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Ontario Task Force
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in Agriculture

Groupe d'étude de l'Ontario
sur la santé et la sécurité
dans l'agriculture

Background
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# Health of Persons Engaged in Farm Work

A joint project of the Ministries
of Agriculture and Food and Labour

Un projet commun du Ministère
de l'Agriculture et l'Alimentation
et du Ministère du Travail

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# HEALTH OF PERSONS ENGAGED IN FARM WORK

A BACKGROUND LITERATURE REVIEW PREPARED

BY

THE OCCUPATIONAL HEALTH PROGRAM

MCMASTER UNIVERSITY, HAMILTON, ONTARIO

FOR

THE ONTARIO TASK FORCE ON HEALTH AND SAFETY IN AGRICULTURE

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## HEALTH OF PERSONS ENGAGED IN FARM WORK

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## CHAPTER FOUR CANCER AND FARM WORK

# EXECUTIVE SUMMARY

The objective of this literature search on the health of persons engaged in agricultural work with an analysis relating to the findings to Ontario is in accordance with the request for proposals published by the Ontario Task Force on Health and Safety in Agriculture in July, 1984. The tasks to be completed by the Occupational Health Program, McMaster University were:

1. To assemble and review relevant literature concerning farm work-related injuries and illnesses.
2. To relate the findings to agricultural conditions in Ontario.
3. To identify priorities requiring further detailed study and analysis.

The first objective was acheived by a comprehensive review of relevant scientific literature concerning disease and injury of farm workers published in the scientific literature. Additional information was obtained from agricultural research centres and government sources. From information already obtained concerning the pattern of farming in Ontario it was possible to indicate areas likely to require detailed study. By identifying the most serious potential problems and also those which are most likely to respond to preventive measures, specific recommendations are proposed.

These recommendations are as follows:

RECOMMENDATION 1

A detailed survey regarding exposure to pesticides and organic chemicals in farm work be carried out across Ontario to identify populations at risk of adverse health effects.

RECOMMENDATION 2

A health data collection system for agricultural health and safety be established to detect potential adverse health effects of farm work in Ontario.

RECOMMENDATION 3

An agricultural health and safety research program be organized within an Ontario University to carry out descriptive and analytical epidemiological studies of the health of persons engaged in farm work.

RECOMMENDATION 4

An intensive educational program for family physicians, medical officers of health, physicians in postgraduate training, and medical and nursing students concerning occupational health and safety in agriculture be initiated in Ontario.

RECOMMENDATION 5

Preventive interventions including legislation and community-based worker education pertaining to the protection of the health of persons engaged in farm work in Ontario be brought into effect.

# CHAPTER ONE

# BACKGROUND

## Introduction

The following background paper relative to the Health of Persons Engaged in Farm Work, was prepared in response to a request from Dr. N.R. Richards, Chairman of the Ontario Task Force on Health and Safety in Agriculture and its members.

## Terms of Reference

The Terms of Reference for the Task Force are included here as supportive preamble to the Terms of Reference for this background paper. The Terms of Reference for this paper as developed by the Occupational Health Program, McMaster University and the Task Force follow those of the Task Force in this chapter.

**Terms of Reference for the Task Force on Health and Safety in Agriculture**

1. The Task Force is established by the Minister of Agriculture and Food and the Minister of Labour of the Province of Ontario and its members will be appointed by documents signed by both Ministers.

2. The Task Force is constituted to carry out the task defined in these Terms of Reference and will cease to exist when that task is completed.

3. The function of the Task Force will be to investigate and report on the need for protection of the health and safety of farmers, farm workers and members of farm families engaged in farm work.

(a) the nature of occupational health and safety hazards in agriculture;

(b) where the need for protection exists, that is, what occupations, farm work activities and types of farming;

(c) how the occupational health and safety experiences of persons engaged in on-farm work vary by age, form of attachment to the industry, length of service and other relevant personal variables;

(d) the problems of defining a farming operation and a farm workplace;

(e) mechanisms for providing protection against health and safety hazards in farm work; and

(f) if the conclusion is that legislation is required, the areas to be addressed.

4. The Task Force will present its findings to the Ministers of Agriculture and Food and of Labour, in a fully documented final report and, as deemed appropriate, interim reports will be made to a joint steering committee of officials drawn from both Ministries.

5. The study will be initiated in October 1983, and every reasonable effort will be made to make the final report available during July 1985.

6. The Task Force will obtain information necessary to its assignment through library research, receipt of presentations from farmers and others interested, and consultation with persons who are knowledgeable about farm health and safety in Ontario and other jurisdictions. The Ministries will provide research resources to assemble, analyze and document information required by the Task Force.

7. The Ministries will provide assistance on legal matters as required by the Task Force.

8. The two Ministries will share equally the costs incurred by the Task Force.

Task Force members are:

Chairman

Dr. N. Richard Richards, 59 Green Street, Guelph

Members

Ron Cameron, R.R. #6, Thamesville

Rejean Leclerc, R.R. #3, Casselman

Peter Lindley, 219 Book Road West, Ancaster

Alphonse Meunier, R.R. #2, Blackstock

Roger Morrison, R.R. #4, Seaforth

Lyle Vanclief, R.R. #1, Ameliasburg

**Terms of Reference for the Background Paper on the Health of Persons Engaged in Farm Work**

One of the objectives of the Task Force was to identify the relationship between farm population, farm labour force, employment in agriculture, types of agriculture across Ontario and experience in health and safety. Agriculture is defined as the work of cultivating the soil, producing crops and raising livestock. Farm work refers to any work done on the farm other than in the house, house yard and farm family garden. This would include off-farm work as well, such as moving equipment or crops on a highway between two parts of a farm or to processing plants or markets.

To build up a profile of the farm labour force and to relate this to risk is difficult because the farm as a geographic location is a place of business and a place to live, and family members can be exposed to agricultural risks even when not involved in the farm business. The work time of family members is difficult to determine particularly if the family labour is unpaid. The supply of, and demand for hired labour fluctuates with the largest part of the total labour supply working on a seasonal basis. Haslett (1984) classified farmers without hired labour as own account farmers and farmers with hired labour as employers. Workers other than farmers were divided into two groups, hired and unpaid. Because of the volume of the

literature reviewed here no attempt was made to categorize each study according to these definitions. We did, however, adhere to the terminology that was used within each individual paper.

A comprehensive review of the scientific literature through the computer links maintained by the Occupational Health Program at McMaster University and also through our link with the Canadian Centre for Occupational Health and Safety was carried out. The data banks included in this survey: Agricola (Dialog and BRS System); Biosis; Cab Abstract; Cancerlit; Centre Internationale de Securite et d'Hygiene du Travail (CIS); Chemline; Current Research Information System/United States Department of Agriculture (CRIS/USDA); Embase (Dialog); Food Science and Technology Abstracts; Medline; Nioshtic; Ntis; Sdiline; Toxline, covered the great bulk of material published.

Contact was established with major agricultural research institutes which provided information of an epidemiological type which has not been published in the scientific open literature.

The literature was reviewed as to its scientific merit by methodologies which have been developed within the Department of Clinical Epidemiology and Biostatistics at McMaster University. The farm work-related diseases and injuries are ranked according to their potential for causing serious or lasting effects on health and also for their potential for remedial action. This last point is of considerable importance. Priorities for study at a later date should be given to those health risks which are most likely to respond to preventive action.

The principal author of this report was Dr. John Chong, Assistant Professor in the Department of Clinical Epidemiology and Biostatistics and Occupational Health Program, McMaster University.

## CHAPTER TWO

## RECOMMENDATIONS

It is recommended to the Ontario Task Force on Health and Safety in Agriculture that:

RECOMMENDATION 1

A detailed survey regarding exposure to pesticides and organic chemicals in farm work be carried out across Ontario to identify populations at risk of adverse health effects.

The exposure information concerning persons engaged in farm work in Ontario is only at a general level. Population groups potentially exposed to various types of agricultural chemicals can be identified through data from Agriculture Canada, Statistics Canada, and the Ontario Ministry of Agriculture and Food.

For example, from the above sources and Dr. Ross Hall of McMaster University, a profile of pesticide usage in Ontario can be made. The following table summarizes this information:

| Class | Major Chemicals Used | Amount Sold/used (tonnes) | Acreage treated | Crops |
|---|---|---|---|---|
| Organophos-phates | chlorpyrifos | 22.9 | | tobacco |
| | trichlorfon | 35.5 | | tobacco |
| | phorate | 29.0 | | corn |
| | azinphos-methyl | 25.2 | | fruit(apples) |
| | phosalone | 20.2 | | fruit |
| | phosmet | 29.0 | | fruit |
| | malathion | | | mushrooms |
| | diazinon | | | vegetables |
| Carbamates | methomyl | 11.3 | | tobacco |
| | carbaryl | 33.1 | | fruit |
| | | 11.6 | | vegetables |
| | aldicarb | 22.6 | | vegetables |
| | carbofuran | 18.5 | | vegetables |
| | aminocarb | 0.43 | | forest |
| | acephate | | | tobacco |
| Thiocarbamates | mancozeb and dinocap | 59.3 | | fruit |
| | metiram | 39.3 | | fruit |
| | | 43.0 | | vegetables |
| | mancozeb | 24.5 | | vegetables |

| Class | Major Chemicals Used | Amount Sold/used (tonnes) | Acreage treated | Crops |
|---|---|---|---|---|
| organo-chlorines | dichloropropane and/or dichlor-opropene (fumigant) | 1156.6 | 63185.2 | tobacco |
| Fungicides | captan | 54.3 | | fruit |
| | captafol | 35.9 | | vegetables |
| | chlorothalonil | 32.5 | | vegetables |
| | benomyl | | | |
| Herbicides | | | | |
| Phenoxys | 2,4-D (and/or 2,4,5-T) | | 50,000 | forest |
| | MCPA | | | wheat, flax |
| Synthetic Pyrethroids | permethrin | | | apples; tomatoes and cucumbers (in greenhouses) |
| | cypermethrin | | | tobacco |
| | deltamethrin | | | cereals |
| | fenvalerate | | | fruit (apples) |
| Others | EPTC | 16.1 | | Vegetables |
| | maleic hydrazide | 22.1 | | Vegetables |
| | atrazine | 1411.0 | | field crops (corn) |
| | butylate | 734.0 | | " |
| | cyarazene | 505 | | " |
| | alachlor | 463 | | corn, soybean |
| | trifluralin | | | soybeans, tomatoes |
| Fumigants | aluminum phosphide | | | grains |
| | methyl bromide | | | grains |
| | ethylene dibromide | | | grains |
| Others | sulphur | 23.6 | | fruit |
| | copper sulfate | 25.2 | | vegetables |
| | B.t. (b) | | | forest |
| Growth Regu-lator | n-decanol | | | tobacco |

a) This information was collected from OMAF (1978) (1978 data); Agriculture Canada (1983b).

b) Bacillus thuringiensis; a biological insecticide.

This data is far from providing the quantitative exposure information required for proper epidemiological studies and risk assessment. General populations at risk could be more easily identified if centralized information on target pests and the time and manner in which the pesticides were applied was available. Information on the formulation and suppliers of

agricultural chemicals would augment estimations of dose as the toxicity of various compounds often differs with different formulations. Even more specific information on dose must be collected through studies using environmental and biological monitoring.

We cannot be certain of the adequate protection of the health of farmers, farm workers and members of farm families engaged in farm work without reliable and valid exposure asertainment regarding known and potentially hazardous substances.

## RECOMMENDATION 2

**A health data collection system for agricultural health and safety be established to detect adverse health effects of farm work in Ontario.**

In order to detect the general patterns of disease in the Ontario farming population and then be able to generate hypotheses as to causal factors requires a health data collection system. The possible sources of data for such a system could be collected from existing sources listed below, however many shortcomings pertaining to agricultural health and safety exist.

Accessible sources of Health Data in Ontario

| Source | Level of Information |
|---|---|
| Hospital Medical Records Institute | - inpatient information (does not include emergency patients)<br>- diagnoses only, no symptomatology<br>- no information on occupation<br>- not specific to chemical, only to group<br>- appears to be mostly "home" accidents |
| Hospital Separations | - same data as HMRI |
| Morbidity and Mortality Statistics (Statistics Canada) | - same data as HMRI |

| | |
|---|---|
| Poison Control Centres (Health and Welfare Canada) | - symptoms of poisonings<br>- centralized information in Ottawa<br>- most information is from "home" use<br>- no information on occupation |
| Ontario Hospitals Insurance Plan | - level of information differs among physicians<br>- most detailed systems include information on diagnoses and physician services |
| Workers' Compensation Board | - most farmers are not part of a WCB although some Ontario farmers are |
| Ontario Cancer Treatment and Research Foundation | - very little linkage to occupation or chemical exposure |
| Ontario Ministry of Health | |
| Disease Control and Epidemiology Sentinel Physician Program | - covers only infectious diseases<br>- surveillance system |

The net result of inadequate and poor quality data is the under-reporting of health events which may be causally linked to exposures during farm work. For example to recognize cases of acute pesticide poisoning, both the medical profession and pesticide users must be aware of the toxicological effects of these substances. The events must then be recorded in such a way that the information from the emergency room includes the occupation of the individual poisoned and the nature and circumstances of the toxic exposure. Currently misdiagnoses and misclassification of the cause of the health effect or death are common across the different sources of health information.

Of particular concern are agricultural workers who are recent immigrants to Ontario. Because many of them do not speak English and have little job security, they are unlikely to report a health effect to an institution of authority.

Chronic health effects from exposures during farm work are difficult to monitor due to long latency periods before the the appearance of the effects. Examples drawn from this

literature review are cancer, neurological disorders and adverse reproductive outcomes.

Without such a health information system that will provide the required information, appropriate analytic epidemiological studies will be severely limited. The design and implementation of preventive interventions may be as a result ineffective, inefficient, and unacceptable.

## RECOMMENDATION 3

**An agricultural health and safety research program be organized within an Ontario University to carry out descriptive and analytical epidemiological studies of the health of persons engaged in farm work.**

This document reviews in great detail the scientific literature concerning the health of persons engaged in farm work. Some aspects of this relationship have been well explored such as respiratory diseases and acute neurological effects of organophosphates. Unfortunately, the literature is inadequate and flawed from the methodological point of view in other conditions. Most striking is the lack of information specifically related to farming in Ontario.

The advantage of creating a centre of excellence for epidemiological research in agricultural health and safety within an existing Ontario University research program will be that problems pertaining to Ontario can be explored in a rigorous and methodologically sound fashion with comprehensive planning of priorities. With the exception of a few places in the world, epidemiological research in this area is carried out in a haphazard and disorganized way such that the needs and priorities of the population at risk are not met.

RECOMMENDATION 4

**An intensive educational program for family physicians, medical officers of health, physicians in postgraduate training, and medical and nursing students concerning occupational health and safety in agriculture be initiated in Ontario.**

The under-recognition of occupational exposures as a determinant of illness rests largely with the medical profession. The curriculum content of undergraduate and postgraduate training programs are governed by factors relating to the health care system rather than the health needs of the population being served by the system.

The lack of professional training opportunities has only been recently acknowledged, for example, by the Advisory Council on Occupational Health and Safety. Programs are available at McMaster University and the University of Toronto for postgraduate physicians interested in a career in occupational medicine. Most of these graduates find employment within industry and government, but without a system of delivery of health services targetted at the agricultural sector, few of these individuals will be in a position to address the issue of concern.

Medical education in occupational health must begin early in training and not wait until clinical attitudes and behaviours are constrained by other commitments. At McMaster University, a major initiative to integrate occupational health content into the core problem-based curriculum is underway, utilizing resources in the community and industry. Postgraduate programs for residents in family medicine and community medicine are available. A project to establish a long distance instruction program for remote family physicians and medical officers of health has been ongoing. The educational needs of these groups have been surveyed to facilitate the design of self-instruction modules on priority topics in occupational health. A large program for occupational health nurses has been highly successful.

By utilizing existing resources and programs in Ontario, a major educational intervention could be designed, evaluated, and implemented in the near future. Only until then can the problem of recognition of health problems related to farm work be addressed.

RECOMMENDATION 5

Preventive interventions including legislation and community-based worker education pertaining to the protection of the health of persons engaged in farm work in Ontario be brought into effect.

Interventions aimed at protecting the health of workers must be characterized by clear and unequivocal procedures which are often introduced as legislation coupled with adequate training of those individuals to whom the procedures and/or legislation applies.

This review of the literature covers the broad scope of health effects related to farming. By introducing legislation that will require the assessment of exposure to hazardous substances, control of exposure to hazardous substances, and mechanisms of informing risk, reporting adverse health events, and monitoring of populations at risk, many of the problems regarding the health of persons engaged in farm work in Ontario could be ameliorated.

# CHAPTER THREE

## BURDEN OF ILLNESS AMONG PERSONS ENGAGED IN FARM WORK

### General Epidemiological Approaches

#### Introduction

Epidemiology is the study of the pattern of diseases that occur in human populations and the factors that influence them. Traditionally it means the study of epidemics, and was used primarily to identify the factors that caused infectious diseases. Epidemiology was first used in 1532 by a London physician who studied the geographical patterns of the weekly cases of cholera to discover a polluted water source as the cause of the epidemic. Over time epidemiologists haved refined their skills and epidemiology has become an important tool in the study of disease (morbidity) and death (mortality) caused by agents in the environment and more recently in the workplace.

The epidemiological approach contributes to the attainment of five main goals:

1. measurement of the burden and distribution of illness in a population at risk from occupational and environmental hazards;

2. identification and measurement of known and potential causal factors for occupational and environmental illness;

3. recognition and monitoring of illnesses in populations at risk from occupational and environmental hazards;

4. assessing the magnitude of risk and dose-response relationship of occupational and environmental hazards; and

5. evaluation of the efficacy, effectiveness, and efficiency of preventive interventions designed to reduce disease burden and maldistribution.

The following approaches can be used to assess the adverse effects of occupational and environmental hazards.

## Descriptive (Hypothesis-generating) Studies

Descriptive studies are useful for the generating of a hypothesis, but alone, they are not a means of testing an etiological hypothesis. These types of studies fall into three main categories.

### Case Reports

The description of cases of illnesses that relate to a particular exposure rouses the suspicion that the illness may have occupational or environmental origins.

### Surveillance

The value of monitoring activities, which should be continuous programs with rapid reporting and periodic reviews and analyses of data, is to provide background for testing hypotheses. For example in Scandinavian countries, workers are registered according to occupation. This computerized registry can be linked to the occurrence of specific cancers and developmental hazards such as abortions and malformations, to identify populations at risk. Once a registry has been established, such data analysis is rapid and relatively inexpensive. The shortcomings of this approach are that some occupations may not be accurately represented such as migrant workers or part-time and seasonal workers.

It is possible to compare data collected over a certain period with standardized records. The technique can be coupled to analytical study designs such as large-scale case-control studies. These methods will produce more reliable results if population-wide surveillance systems are established. Surveillance should be regarded as an essential descriptive element in further epidemiological investigation rather than a separate entity for evaluating an occupational or environmental hazard and/or subsequent risk.

### Correlation Studies

Correlation studies are concerned with the pattern of distribution of any health condition, as well as variations in the occurrence of a condition in relation to time, space, and individual characteristics, in populations with various levels of exposure to occupational or environmental hazards. Non-causal correlations cannot be ruled out as confounding factors are difficult to control.

### Analytical (Hypothesis-testing) Studies

These studies help in establishing cause-effect relationships and in the estimation of their magnitude.

### Cross-sectional Studies

The objective of cross-sectional or prevalence studies is to determine the prevalence rate of a condition in a given population. The burden and distribution of a condition are described and its association with a potential causal factor is determined. Often a prevalence study constitutes the first phase of a prospective study and is usually conducted on a representative sample of the population, within a short period of time, to provide an "instantaneous" image about diseased and healthy groups within that population. The population and the variables to be considered must be very well defined.

### Case-control Studies

In case-control studies, which supplement hypothesis-generating studies, the frequency of conditions and the extent of exposures to a potential hazard are compared with those in an unaffected control group. The affected individual is the starting point, while the control group may be selected from unaffected individuals or those with another type of condition. The latter type of control group has the advantage of potentially controlling for recall bias. This design is suited for the study

of rare events, but is often limited by inadequate data to ascertain occupational and environmental exposures.

## Cohort Studies

These are prospective studies in which two or more groups of people exposed to different levels, including no exposure, to a potential hazard are followed up, and their health outcomes recorded while controlling for confounding variables. The starting point for the study may be in the past, necessitating adequate exposure data, and then current health status is measured. This is a historical prospective study. If the study is initiated in the present,, sufficient time must pass to allow for the latency period of a chronic disease, which may be twenty years as in the case of many types of cancer. Even though the prospective method tends to be more informative about the quantitative risk associated with exposure to a potential agent, the size of study populations required, difficulty with follow-up of study cohorts and enormous expense in maintaining the study limits the number of these types of investigations. This design can often be improved by combining study populations from several countries, an approach used successfully in the Scandinavian countries.

## Intervention Studies

In these studies, the frequency of a specific disorder in groups where preventive or corrective measures have been applied is compared with that in controls. Intervention studies can be conclusive if they are carefully designed with random allocation.

## Limitations

The major limitations of the epidemiological approach as related to the study of persons engaged in farm work relates to the inadequacy of existing sources of data. In almost all studies of this type, there is a lack of a quantitative assessment of exposure. The environment contains numerous hazards to which people are continually exposed and it is conceivable

that interactions between the exposures may occur in complex ways. It is therefore difficult to isolate an exposure to a single agent, and a dose-response relationship is rarely established. Potentially confounding factors can be controlled only if they are recognized and are measurable. Statistical power is largely determined by the the rate of expected events in the unexposed or general population. Many of the studies reviewed were limited by insufficient power to detect an effect based on sample size considerations.

In spite of the many shortcomings of the quality of evidence relating farm work and health, the scientific literature contains at present important information of both descriptive and analytical types, that is useful to apply to the study of the health of persons engaged in farm work in Ontario. In the following section, the health status of farm workers is reviewed followed by detailed explorations of specific conditions in subsequent chapters.

## Health Status of Persons Engaged in Farm Work

Kraus (1982) describes epidemiologic methods in field studies of agricultural farm workers. There are more agricultural farm workers in the world than any other occupational group. In many respects this group of workers has the broadest and most extensive of occupational exposures to biological, chemical, and physical agents of disease or injury. Although risks associated with certain infectious or chemical agents such as coccidiodes immitis or methyl parathion are well documented from acute episodes, a clear understanding of the full spectrum of health hazards to these workers remains obscure. The reasons for this are numerous, including the wide variety of diseases and different work tasks involved, the highly changeable work environment, the frequency of mobility of work, the absence of high quality medical care, the difficulty of investigators to assess the nature and degree of occupational exposures, and the absence of measurable indices for subtle long-term health effects

from work. These are some of the issues confronting the epidemiologist in designing field studies for this occupational group. This paper addresses these methodological problems, drawing upon the experience of many years of field studies aimed at assessing health effects from usual agricultural farm work. Methods to improve field worker monitoring, elucidation of subtle but avoidable biases in epidemiologic studies of these workers, and refinements in analytic approaches are some of the topics presented in this paper. Similar challenges confront an occupational epidemiologist faced with the study of health risks among Ontario farmworkers due to inadequate and unreliable sources of data.

Sullivan et al (1979) did a study of a selection of farms in the counties of Southwestern Ontario near The University of Western Ontario during summer 1979. After familiarizing themselves by literature study of the types of occupational health and safety problems likely to be encountered, a group of students conducted interviews with farmers and collected information from other sources. The results of the farmer interviews have been described as case studies. Traumatic injuries, mainly from the use of machinery with accidents such as tractor roll over and entanglement in moving parts were the most evident and dramatic hazards on farms. A significant proportion of these result in death. Other causes of death and injury are asphyxiation by toxic gases, falls, crushing by falling trees, attacks by animals and similar risks. Less dramatic, but possibly greater causes of disability are toxic pesticides, inorganic and organic dusts including allergens, infectious diseases transmitted by animals and noise and vibrations from machinery. Much of the information relating to these types of problems was scanty and difficult to elucidate. The general conclusion obtained by the study was that the health consequences of these hazards were probably much under-estimated.

Gallagher et al (1984) described occupational mortality patterns among British Columbia farmworkers. Proportional mortality ratios (PMRs) were calculated for 2,328 British Columbia farm workers who died at age 20 years or over during the

period 1950 through 1978. Significantly fewer deaths than expected from degenerative heart disease (PMR = 91, $p < .01$) and from all cancers combined (PMR = 78, $p <.001$) were observed. Deaths from bronchitis and emphysema (PMR = 70, $p < .05$) were also fewer than anticipated. Elevated risks of death were found for accidents (PMR = 129, $p < .001$), for homicide (PMR = 242, $p <.01$), and for pneumonia (PMR = 146, $P < .001$).

Stubbs et al (1984) conducted a proportionate mortality analysis of all deaths recorded during 1978/1979 among California farm workers and farm owner/managers. For farm workers they found proportional mortality ratios (PMRs) which were consistently elevated for all race and sex categories in which there were 6 or more decedents for deaths due to motor vehicle accidents, all respiratory disease, and all infective and parasitic diseases. The PMRs for the former three causes of death were also found to be elevated across several race and sex categories for farm owner/managers. They also found a significant and consistent deficit of deaths among farm workers and farm owner/managers due to arteriosclerotic heart disease. The proportionate cancer mortality ratios (PCMRs) for cancer of the stomach and cancer of other lymphatic tissue were elevated, although not necessarily statistically significantly, for several race and sex categories among farm workers and farm owner/managers. The PCMR for cancer of the cervix was statistically significant for white female farmworkers.

Burmeister & Morgan (1982) found that death certificate analyses of white California males aged 20 through 64 dying from 1959 through 1961 indicated unusually high mortality rates in farm laborers from respiratory diseases and accidents. To determine whether this mortality pattern is pervasive among agriculturally employed workers, similar analyses in Iowa from 1971 through 1978 were completed. Only mortality from work-related accidents was found to be excessive; respiratory disease deaths were no more frequent than among the general population. The reason for high respiratory disease mortality in California remains unknown. The two worker populations differ with respect

to ethnic background, socioeconomic status, mobility and accessibility of medical care. Worker exposures to agricultural chemicals and to dust are substantial in both regions, but are qualitatively different. One or more of these factors could account for the different rates of respiratory disease mortality.

Carlson & Petersen (1978) examined the mortality of white male farm laborers and farm operators in California for the years 1959 to 1961. Cause-specific mortality rates were calculated in order to identify diseases which might be of occupational importance. The mortality rate from respiratory diseases in the farm laborer groups (employees) was triple the rate in the farm management group (employers or self-employed individuals). Accidental deaths were also increased in the farm laborer group. Hazards of the agricultural industry which could contribute to accidents and respiratory disease were reviewed.

Burmeister (1975) reported a survey of the causes of death of males and females to give some estimates of the relative health of persons living in rural and urban areas, and hence of the relative health of farmers. There are differences in death rates for males and females, and the accident rates are consistently and significantly higher for male rural residents. Death rates for farmers and farm managers are compared with those for other occupations. Farmers and farm managers have higher death rates than others except laborers (except farm), craftsmen, and foremen and kindred. Generally rural places of residence are healthier than urban, and the health of rural populations appears related to the strength of the agricultural economy.

Milham (1976) analyzed the occupational and cause-of-death information on about 300,000 Washington State male (age 20+) death records for the years 1950-1971 using an age and year of death standardized proportionate mortality ratio approach. A detailed cause of death analysis (160 causes) is published for each of 194 occupational classes. The occupational mortality findings are compared with those of the Registrar General, for England and Wales (1,2), and with the one 1950 U.S. study (3). In general, the Washington State mortality pattern is consistent

with the published occupational mortality literature, but new occupational mortality associations are present which warrant follow up.

Pomhren et al (1982) observed that an analysis of 62,000 deaths in Iowa men aged 20 to 64 years from 1964 to 1978 indicates that Iowa farm men younger than 65 years have lower than expected mortality for all causes and for ischemic heart disease. Using data gathered by the Iowa Lipid Research Clinics (LRC) Program Prevalence Study, they compared levels of known cardiovascular risk factors in farmers with those of nonfarmers residing in the same rural county. Farm men smoked less frequently (19% v 44%) and engaged in exercise more frequently (83% v 40%) than nonfarmers. Treadmill performance in farm men indicates a higher level of fitness in farmers. Farm people consumed more total calories and cholesterol, but drank less alcohol than nonfarmers. Farm men had significantly higher serum cholesterol levels. High-density lipoprotein cholesterol levels were also higher in farmers. However, when adjusted for age and exercise status, farmers and nonfarmers had similar lipid levels. The results of the LRC survey suggest that the lower mortality rates of Iowa farmers are a reflection of a life-style that includes vigorous exercise and little consumption of alcohol and tobacco.

Blair and Hayes (1982) looked at causes of death among 5016 white male veterinarians identified from obituary listings in the Journal of the American Veterinary Medical Association and compared them to a distribution based on the general U.S.A. population. Proportions of deaths were significantly elevated for cancers of the lymphatic and haematopoietic system, colon, brain and skin. Fewer deaths were observed than expected for cancers of the stomach and lung. Although socioeconomic and methodological factors may be involved, the patterns suggest that sunlight exposure is responsible for the excess of skin cancer among veterinarians whose practices are not exclusively limited to small animals and ionizing radiation exposure contributes to the excess of leukaemia among veterinarians practising during

years when diagnostic radiology became widely used. Mortality was also high for motor vehicle accidents and suicides, but low for diseases of the respiratory system.

Bleiweis et al (1977) questioned farm workers, representing 65% of the migrant work force in the St. Johns River basin agricultural area of north Florida, in 1973-1974 about their own and their families' health status and about their use of professional health care services and facilities. The facilities available for use by this population included 22 physicians in private practice, two hospitals, three public health clinics, and two health clinics operated for migrants. Most contacts made by the migrant farm workers were with the health care professionals in the public facilities, primarily those in the migrant health clinics. The average number of visits made by migrant farm worker heads of households to a physician each year was 3.5 visits. In 1971, the National Health Survey reported an average of 4.9 physician visits for all U.S. citizens. The major factors that affected utilization were the presence of an acute medical condition and the perception of being in poor health. The factors that generally have been thought of as impediments to seeking health care, such as transportation, the presence of children in the household, and a lack of education, were found to be of little import. The acute disease conditions that were most frequently reported by these migrant workers as the reason for their contacts included respiratory illnesses, digestive system problems, injuries, and musculoskeletal problems. The chronic conditions included heart disease and hypertension, musculoskeletal disorders, digestive system problems, and genitourinary problems. Little use was made of dental services, except for tooth extractions.

Husman et al (1982) described farmers' work and health 1979, based on the results of a postal survey conducted in the winter of 1979-1980. The survey was done by the Research Institute for Social Security of the Social Insurance Institution of Finland in collaboration with the Kuopio Regional Institute of Occupational Health and the National Board of Health. The purpose of the study was to provide information for the planning and the

evaluation of the experiment on the organization of farmers' occupational health. Most of the 12,056 farmers included in the study were occupied in livestock production. Grain production, forestry, and pig raising were the most common types of farm production after livestock production. Most of the work required in livestock raising was manual, whereas most of the work required in grain production was mechanized. About 57% of the sample reported chronic illness. Of the chronic illnesses one-third consisted of diseases of the musculoskeletal system, one-fifth of cardiovascular diseases, and about 7% were diseases of the respiratory system. About half of those with a chronic disease reported a reduced work ability or complete disability. Of all the surveyed, about every fourth farmer had reduced his work load or changed his work tasks due to illness, mostly due to the diseases of the musculoskeletal system. Performing daily tasks was the most frequently reported cause for insufficient care of illness. Health examinations, medical care, and information about work-related risks were among the most common expectations of the statutory occupational health services. They concluded that the occupational health services of farmers should be aimed at the prevention of accidents and diseases of the skin, respiratory system, and musculoskeletal system.

Navakatikian et al (1980) showed that combined clinical and hygienic studies revealed a relationship of certain types of abnormality to the occupation and duration of work of agricultural workers. Among machine operators, the rates of chronic bronchitis, digestive disturbances, and hearing loss have now decreased, whereas cardiovascular and nervous disorders have shown an increasing trend, these changes in morbidity rates being associated with improved design of machines on the one hand and with intensification of work on the other. The changes recorded in the cardiovascular, respiratory, and sympathoadrenal systems and in the adrenal cortex were related to the occupation, the season of work, and work intensity. Multiple regression and discriminant analyses established a correlation of pathologic and functional changes in the cardiovascular system with the working conditions of machine operators.

Anders Thelin (1980) randomly selected 221 farmers in Kronoberg County, Sweden, and interviewed and examined 191 with the aim to disclose and to investigate health risks within Swedish agriculture. The mean age of the farmers, 53.8 years, is higher than the average for those occupied in industry, but level with the total farming population of Sweden. Production forms, performance, and mechanization agreed well with the conditions in similar areas of the country. Most of those studied were occupied with both farming and forestry. The smokers were fewer than among Swedes in general. Despite that, diseases of the respiratory organs were usual. Twenty per cent had pneumonia and 6% pleurisy. Allergic conditions were found in 13%; 12% had or had had prolonged and severe cough. The farmers were sick-listed less than a randomly selected control group, except for diseases in the respiratory organs and accidents. Rather few farmers had been sick-listed for cardiovascular diseases. The number of farmers with high blood pressure was low (8% > 160/95). Back and joint disorders were reported by a large section of the examined, but diseases in the back and joints did not seem to be more common among farmers than among others in so called heavy occupations. It is not possible to exclude a connection between prolonged tractor driving and an increased risk of back trouble and hip-joint arthrosis. Only 10% of the farmers were free from considerable hearing impairments. About 14% of those studied had strongly reduced hearing. Of those who used chain-saws, 28% showed symptoms of vibration injury. Of those with subjective symptoms who could be examined at the physiological laboratory, 81% showed objective signs of vibration injury. The reported accidents made it possible to calculate that 45 to 60 accidents occur per million working hours in farming, which is considerably more than that reported in official statistics.

Dubrisay and Pages (1978) observed that among 3276 occupational diseases compensated during the last three years in the system of farmers' social protection, infections and parasitic diseases take up by far the first place and represent 82% of the total. Cutaneous manifestations (8%) come next, then intoxications by chemicals (6%), respiratory diseases (2%),

diseases caused by physical agents and postural disturbances represent only (0.6%) of the total.

Lindgren (1975) reported a questionnaire and interview survey of workers and working conditions in agriculture in southern Sweden. The report covers individual occupations (tractor driving, harvesting, spraying, animal husbandry), physical work loads, ergonomic evaluation (tractors, harvest-threshing machines), occupational hazards (acccident statistics, poisoning), health problems, social benefits. Recommendations for improved working conditions (better access to tractors, more room in the driver's seat, no restrictions to field of vision, damping of vibration of all farm equipment, more space to service equipment, etc.). Sources of information for accident prevention and health protection are listed.

## Scope of Health Problems Among Farmworkers from Agricultural Chemicals

Suskind and Hertzberg (1984) conducted a clinical epidemiologic study to determine the long-term health effects of workplace exposure to the process of manufacturing the herbicide (2,4,5-trichlorophenoxy)acetic acid including contaminants such as 2,3,7,8-tetrachlorodibenzo-p-dioxin. The population consisted of two cohorts: 204 clearly exposed and 163 not exposed. Among the exposed, clinical evidence of chloracne persisted in 55.7%. None of the not exposed experienced chloracne development. An association was found between the persistence of chloracne and the presence and severity of actinic elastosis of the skin. There is an association between exposure and the history of gastrointestinal tract ulcer. Pulmonary function values among those who were exposed and who currently smoked were lower than those who were not exposed and who currently smoked. The data assembled in the study indicate no evidence of increased risk for cardiovascular disease, hepatic disease, renal damage, or central or peripheral nervous system problems.

Wong et al (1984) conducted a historical prospective mortality study on 3579 white male workers employed between 1935 and 1976 with potential exposures to brominated compounds including 1,2-dibromo-3-chloropropane (DBCP), Tris (2,3-dibromopropyl) phosphate, polybrominated biphenyls (PBB), various organic and inorganic bromides, and DDT. The vital status as of 31 December 1976 was determined for 3384 (95%) of these workers: 2806 (79%) were still living and 578 (16%) had died. Death certificates were obtained for 541 deaths (94% of all deaths). The mortality experience of the entire cohort and several subcohorts was compared with that of United States white men adjusted for age and calendar time. The comparison statistic was the commonly used standardised mortality ratio (SMR). Historical industrial hygiene data were not available, and the workers were classified by their work areas or departments in order to estimate their potential exposures. Overall mortality for the entire cohort and several subgroups was significantly lower than expected. For the entire cohort, significant mortality deficits were observed in diseases of the circulatory system, non-malignant respiratory disease, and diseases of the digestive system. On the other hand, mortality from diabetes mellitus was significantly raised for the cohort. No significant overall or cause-specific mortality excess was detected among employees potentially exposed to either TRIS or DDT. A significant mortality excess due to diseases of the circulatory system was observed among workers potentially exposed to DBCP. Mortality from testicular cancer was significantly higher than expected among those potentially exposed to other organic bromides. The common potential exposure of those who had died of testicular cancer was methyl bromide. Owing to the lack of accurate historical exposure information and the fact that many workers were potentially exposed to a multitude of chemicals, it is difficult to draw definitive statements on the causations of the observed mortality excesses.

Riihimaki et al (1982) reported on an ongoing prospective cohort study. The mortality experience in a cohort of 1,926 men who had sprayed 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) during 1955-1971 has been followed prospectively from 1972 to 1980. The total phenoxy acid

exposure was generally rather low because the duration of work had mostly been less than two months. In 1972-1976 mortality from all natural causes in the cohort was only 54% of the expected value (based on age-specific rates for the general population), and in the succeeding 4-a period 81% of the expected value. In the assessment of cancer, mortality allowance was made for 10- and 15-year periods of latency between the first exposure and the start of the recording of vital status during the follow-up. No increase in cancer mortality was detected, and the distribution of cancer types was unremarkable. No cases of death from lymphomas or soft tissue sarcomas were found. The study results must, however, be viewed with great caution owing to the small size of the cohort, the low past exposure, and the brief follow-up period.

Lings (1982) saw a fruit-grower with large, atypical lung infiltrations and lung fibrosis. This triggered off an investigation of fruit-growers during the spraying season. An interview was carried out together with a Wright peak flow meter test and an x-ray examination of the chest. No fewer than 156 spray preparations were used by the group; individual fruit-growers used between three and 27. In connection with spraying, 41% of subjects had one or other type of symptom; peak flow was reduced in 19% and x-ray changes were seen in 24%. A questionnaire was returned by 132 of 235 farmers. Of these, 60 had worked with biocides, 72 had not. A non-significant higher frequency of symptoms was found among those who used biocides. The results would indicate that biocides (or "pesticides") can give rise to a lung disease, "biocide lung", which comprises (1) pneumonia, radiologically demonstrable by more or less transient round infiltrations and (2) chronic progressive lung fibrosis.

Ditraglia et al (1981) conducted a retrospective cohort study to examine the mortality of workers employed in the manufacture of the chlorinated hydrocarbon pesticides, chlordane, heptachlor, dichloro-diphenyl-trichloro-ethane (DDT) and aldrin/dieldrin/endrin. Four manufacturing plants were selected for study, and each cohort included all workers employed for at least six

months prior to Januray 1964. The entire study group totaled approximately 2,100 individuals. Vital status ascertainment for these cohorts ranged from 90 to 97% complete; the cut-off date for follow-up was 31 December 1976. In general there were too few deaths in this study on which to draw any meaningful conclusions. The standardized mortality ratio (SMR) for all causes in each cohort was below the expected level (100) and ranged from 66 to 82, probably a reflection of the "healthy worker effect." For "all malignant neoplasms" the SMRs ranged from 68 to 91 and for respiratory cancer from 55 to 132. In the aldrin/dieldrin/endrin cohort observed deaths due to pneumonia and "other respiratory diseases" were significantly above the expected number of deaths. For several other specific cancer sites (stomach in plant 1, esophogus, rectum, liver and lymphatic/hematopoietic system in plant 3), the observed deaths were more than the expected number and should be examined in more detail. It is recommended that these cohorts be followed for several more years and the mortality patterns be reexamined.

Morgan et al (1980) utilized cause-of-death information and responses to questionnaires addressed to survivors, mortalities and health impairments in a cohort of workers occupationally exposed to pesticides. These were compared to occurrences in workers not pesticide exposed, over the period 1971-1977. Seventy-two percent of 2,620 pesticide-exposed workers, and 75% of 1,049 "controls", recruited in 1971-73, were accounted for either by returned questionnaire or mortality. Disease incidence rates were studied in relation to broadly defined occupational subclasses, and to serum concentrations of organochlorine pesticides (OCL) measured at the time of recruitment.

Death by accidental trauma was unusually frequent among pesticide applicators. Mortalities from cancer and arteriosclerosis were not detectably different from those observed in the controls. Among survivors, dermatitis and skin cancer were unusually common in pest-control operators. Internal cancer was no more frequent in the intensively pesticide-exposed workers than in the controls, but it appeared to occur at an unusually high rate in workers characterized as "possibly pesticide-exposed".

Wang and MacMahon (1979) obtained information on a cohort of professional pesticide applicators which will be followed prospectively. The cohort consists of 16,126 males employed for three months or more between 1967 and 1976 by any of three nationwide pest control companies. Deaths which occurred between 1967 and 1976 were reported by the Social Security Administration as a result of a search of its records. Overall, 311 deaths were ascertained, giving a standardized mortality ratio (SMR) of 84. SMRs were over 100 for three causes of death - cancer of the lung (115), cancer of the skin (173) and cancer of the bladder (277). The confidence intervals of two of these ratios include 100, and the observed numbers therefore do not differ significantly from those expected. For bladder cancer the excess is on the border of statistical significance ($P < 0.05$). The excess of deaths from lung cancer was not seen for applicators classified as termite control operators, a group more likely to be exposed to chlordane and heptachlor. There were significantly low SMRs for cancer of the digestive organs (46) and for other diseases of the digestive (55) and respiratory (29) systems. Deaths from cerebrovascular disease were also less than expected, though not significantly so.

Gehlbach and Williams (1977) reported in four years, 218 pesticide exposures among North Carolina children. Epidemiologic follow-up revealed 50 symptomatic cases with nine fatalities. Mean age of exposed children was 27 months; boys were involved twice as frequently as girls. Agents most often implicated were anticoagulant rodenticides (17%) and organophosphate insecticides (16%). Sixty-eight percent of exposures were to products intended for household use. Special characteristics of pesticides that contribute to morbidity include exceptional toxicity, dermal penetration, and frequent application as food baits. Exposure histories indicate that high petroleum distillate content often adds to product toxicity.

Bogden et al (1975) attempts to delineate the deleterious effects which pesticide exposure may have on migrant farm workers

in the southern part of New Jersey. Essentially, farm workers in New Jersey are classified into four groups:

1. Day Hauls - residents of New Jersey and Pennsylvania
2. Contract Workers - residents of Puerto Rico
3. Migrant workers from the Eastern Stream of Florida and Texas
4. Resident Walk Ins

During the summer of 1973 the Puerto Rican Congress of New Jersey, in cooperation with the College of Medicine and Dentistry of New Jersey (New Jersey Medical School and Rutgers Medical School) and the East Coast Migrant Health Council sponsored a mobile health screening program for rural poor farm workers in Atlantic, Cumberland, Salem and Gloucester counties, which was funded by the Robert Wood Johnson Foundation of New Jersey.

There are four major categories of pesticides: (1) heavy metal containing substances, (2) chlorinated hydrocarbons, (3) carbamates, and (4) organophosphates. The organophosphate group is perhaps the most important in relation to its effects on migrant farm workers.

In a preliminary investigation, they measured serum cholinesterase activities of a small group of migrants working in New Jersey, as well as those of appropriate controls. These were workers who were experiencing symptoms such as headaches, dizziness, and blurred vision, and had been exposed to organophosphates.

Generally depressed cholinesterase activities were found, with one-third of the migrants having activities below the lower limit of normal - 3.6 U/ml. Clearly this "captive" group stands at risk from the chronic effects of pesticide exposure because of their general lack of awareness of dangers and symptoms, and the lack of availability of treatment. In particular, there may be little opportunity for the improvement of the health of the individual migrant worker because the mobility inherent in his occupation prevents him from receiving continuing medical care from the same sources.

## Summary

It is clear from this review of the general burden of illness of persons engaged in farm work the extreme diversity of health problems that are implicated especially from pesticide exposure. The inadequacies of information pertaining to Ontario are apparent.

## CHAPTER FOUR

## CANCER AND FARM WORK

### Mortality Studies

In a Review of Cancer Mortality in Farmers (1982) prepared by Health and Welfare Canada the finding of excess mortality from certain cancers among farmers is consistent with the hypothesis that agricultural environments contain as yet unidentified agents which may cause the respective cancer. In order to elucidate the nature and distribution of such agents, as well as to study other health problems specific to farmers, Health and Welfare Canada and Statistics Canada initiated a health study of Canadian farmers. Statistics Canada conducts two annual surveys of the Canadian farm population: the farm enumerative survey and the Agriculture enumerative survey.

Three additional health related questions were added to the 1982 survey questionnaires, allowing for the establishment of a cohort of 20,000 farmers, with detailed information on pesticide and farm animal exposure, which can be followed up for mortality experienced by record linkage to Statistics Canada's mortality database. In addition, the feasibility of linking Statistics Canada's farm registry to the mortality database is being assessed.

| Cancer | Male Farm Population | Findings |
|---|---|---|
| Leukemia | California | non sig. increase |
| | Iowa | sig. increase |
| | Wisconsin | non sig. increase |
| | Nebraska | sig. increase |
| | Washington | sig. increase |
| | Minnesota | sig. increase |
| Lymphoma | Iowa | sig. increase |
| | California | non sig. increase |
| Multiple myeloma | Washington | sig. increase |
| | Iowa | sig. increase |
| | California | non sig. increase |
| Central Nervous system | Minnesota | sig. increase |
| | Iowa | non sig. increase |
| Stomach | Iowa | sig. increase |
| Prostate | Iowa | sig. increase |
| Skin | Iowa | non sig. increase |
| Lung | Iowa | sig. increase |
| All sites | California | sig. increase |
| | Iowa | sig. increase |

Semenciw et al (1984) prepared a report on Cancer Mortality in Tiny township, Ontario. The report was prepared as a result of a letter from the Tiny Township Ratepayers' Association. Alarm was expressed concerning the possible health hazards of aerially sprayed pesticides. Death data for 1971-1981 were retrieved from the National Mortality Database of Statistics Canada. Population data were available at five-year intervals from the census. Mortality was assessed using age-standardized mortality rates (ASMRs) and standardized mortality ratios (SMRs) to adjust for any difference in age distributions between the town and the comparison areas.

In 1981 12.9% of the male population of Tiny Township was over the age of 65 compared to 8.5% for the province as a whole. No specific site was statistically significantly elevated. Yearly all-cancer ASMRs for the county revealed no period of 3 or more years in which the county rate was significantly greater than the provincial rate.

Cancers for which any area had an age group where the number of observed deaths was significantly greater than expected at the 0.05 level included digestive tract cancer, ovarian cancer and lymphoid cancer. Women of ages 45-54 in Midland experienced 5 deaths from cancer of the digestive tract while 1.24 were expected based on provincial rates (p=0.02). Women in Tiny township over the age of 65 experienced 4 deaths from ovarian cancer while 0.98 were expected (p=0.03) while for all ages combined, 6 were observed versus 2.02 expected (p=0.03). Two deaths due to lymphoid cancer in the age range 35-44 in Tiny and Penetanguishene combined occurred while 0.15 were expected (p=0.02). These two deaths were coded as residents of Penetanguishene. For males of all ages in the same combined area, there were 10 observed deaths due to lymphoid cancer and 3.91 expected (p=0.01). The residency of five of the deaths was coded as Penetanguishene.

No area or age group experienced statistically significantly elevated SMRs for lung cancer, liver cancer, cancer of the prostate or leukemias. No deaths due to liver cancer occurred between 1976 and 1981 in either Tiny Township or Penetanguishene.

The results of this report indicate that Tiny Township

experienced normal cancer mortality rates during the period 1971-1981. Time trend analysis revealed neither a statistically significant increase over time nor a statistically significant elevation of cancer mortality compared to provincial and national rates for Tiny Township or Simcoe County. No specific site was statistically elevated in more than one age group or at significance level of 0.01 using a Poisson ratio test. The excess of ovarian cancer was restricted to women over the age of 65.

The elevation in lymphoid cancer in males was noteworthy due to its reported association with herbicides in other studies. Thus it was of interest to examine the urban-rural distribution of deaths. Within Tiny and Penetanguishene combined, the excess was mainly in Penetanguishine and amounted to approximately 3 deaths. The occupations were mixed and did not include any for which carcinogenic chemical exposures would be expected. Liver cancer has also been associated with use of herbicides; however, no excess was observed in the study areas.

Gallagher et al (1984) evaluated occupational mortality in agriculture by calculating age-standardized proportional mortality ratios (PMR) for 28,032 male farmers with the use of British Columbia (B.C.) death registrations collected from 1950 to 1978. Farmers had significantly elevated risks of death from cancer of the lip (PMR = 191, P = .05), stomach (PMR = 119, P < 0.0001), and prostate gland (PMR = 113, P < .001). In addition, leukemia was higher than expected (PMR = 122, P < .01), as was aplastic anemia (PMR = 174, P < .01). The elevated risks were fairly consistent over the 29-year period for stomach, prostate gland, and lip cancer, as well as for leukemia. The PMR for aplastic anemia was highest for the years 1950-59 and declined over the next 19 years. Farmers also showed significant mortality deficits for several important cancer sites, including esophagus (PMR = 59, P < .0001), colon (PMR = 84, P < .001), larynx (PMR = 62, P < ,01), and lung (PMR = 66, P > .0001) for the period 1950-78.

Blair et al (1983) evaluated the mortality experience of a

cohort of 3,827 white men licensed to apply pesticides in Florida to investigate health effects associated with chronic exposure to pesticides. Although the overall standardized mortality ratio (SMR) for these pest control-workers was not significantly elevated (SMR = 103), excess deaths were observed for leukemia, particularly acute myeloid leukemia (3 observed vs. 0.9 expected), and cancers of the brain (SMR = 200) and lung (SMR = 135). The risk of lung cancer rose with the number of years licensed with SMR of 101, 155, and 289 among those licensed for less than 10 years, for 10-19 years, and for 20 years or more, respectively. Ratios of directly adjusted rates showed similar patterns with observed-to-expected ratios of 100, 175, and 186 for the length of licensure categories. Mortality from lung cancer was greater among persons first licensed before age 40 (SMR = 234) than among those first licensed after age 40 (SMR = 115). Although information on tobacco use was not available, the increasing risk of lung cancer with number of years licensed and the capacity of certain pesticides to produce neoplasms in laboratory animals suggested that some pesticides may be carcinogenic in humans.

Burmeister et al (1983) completed death certificate analyses of white male Iowans over age 30 who died of multiple myeloma, non-Hodgkin's lymphoma, prostate cancer or stomach cancer between 1964 and 1978. Each case was matched to two controls on age (within two years) at death, county of residence, and year of death. Consideration of usual occupation, as recorded on the death certificate, resulted in the following odds ratios for mortality due to the specified cancers among farmers: multiple myeloma, 1.48; non-Hodgkin's lymphoma, 1.26; prostate cancer, 1.19; and stomach cancer, 1.32. Each is statistically significant ($p < 0.05$). Odds ratios were computed separately for three birth cohorts according to counties stratified by crop and livestock production. Multiple myeloma was elevated in those born after 1890 and was associated with number of egg-laying chickens, hog production, insecticide use, and herbicide use. Non-Hodgkin's lymphoma was elevated in those born before 1901 and was associated with egg-laying chickens, milk products sold, hog production, and herbicide use. Although prostate cancer was

elevated in those born before 1901, it was not associated with any agricultural practice. Stomach cancer was elevated in each birth cohort. It was associated with milk products sold, cattle production, and corn per acre.

Buesching and Wollstadt (1984) mounted an exploratory study to determine if risks for cancer mortality among farmers in northwestern Illinois were similar to those observed in Iowa. They chose for examination a county in northwestern Illinois (Winnebago) with a computerized listing of information from the death certificates available locally covering the years 1973-80. To this listing they added Census Bureau codes for occupation and industry as recorded on the death certificate. In this fashion, 71 white male cancer decedents who were farmers were identified. Person-years at risk for the study population were estimated by linear extrapolation of the 1970 and 1980 age-specific Census Bureau figures for the white male rural farm population in the county. The standard population was defined as all white male county residents, with person-years of risk for the standard population estimated by linear extrapolation of 1970 and 1980 age-specific Census Bureau figures. This population had 1,733 cancer deaths during the 8-year period. Analysis consisted of calculation of the standardized mortality ratio (SMR) and chi-square statistic. Only those cancers with an observed frequency of five or more among the study population were included for analysis. Results indicate significantly elevated risk among Winnebago County farmers for non-Hodgkin's lymphoma (SMR=2.65) and prostate cancer (SMR=1.95). Leukemia was also elevated (SMR=2.00), but at a nonsignificant level. The lung cancer SMR, though nonsignificant, indicated decreased risk for farmers (SMR=0.82). Multiple myeloma and cancers of the lip and stomach were too infrequent in the study population for inclusion in the analysis, although the two observed multiple myeloma deaths among the study population suggests that it also may be elevated. The results of the two studies regarding leukemia, lymphoma, and cancers of the lung and prostate gland are similar. The major discrepancy in results is in the rates observed for stomach cancer. In Iowa, stomach cancer was significantly elevated for

farmers and the fifth most frequent cancer overall, whereas in their study only one stomach cancer death among farmers was observed in the 8-year period. The rates observed for cancer of the lymphatic and hematopoietic system in both studies suggest a common risk to farm-related exposures, possibly those associated with fertilizers and pesticides. Studies of incident cases in which more precise diagnostic and exposure information is gathered are necessary to evaluate fully the potential associations between these cancers and farming practices.

Wiklund (1983) examined the Cancer-Environment Registry established in Sweden in 1978. A study of the register revealed that for persons engaged in agricultural work the risk for the most types of cancer was lower than the respective national averages. For cancer of the trachea, bronchus, lung and pleura, the ratio of observed to expected numbers of cases is 0.39 (observed 934, expected 2375). The difference is statistically significant. Primary cancer of the liver and tongue also show less than expected frequency. The risk of cancer of the lip, however, is greater by a factor of almost 2 than the national average, which is consistent with results from other studies.

In the next section, cancer of specific organ sites will be reviewed focusing on the relationship with farm work.

## Hematological Cancer

Brandt (1982) reviewed studies on environmental factors in the etiology of leukemias, myelomas and lymphomas. Ionizing radiation plays a role in the development of acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, myeloma, Hodgkin's disease and non-Hodgkin's lymphomas, but probably none in chronic lymphocytic leukemia. Viral etiology of chronic lymphocytic leukemia in farm workers and of Burkitt's lymphoma and of other non-Hodgkin's lymphomas is suspected. Hodgkin's disease was found to be overrepresented among men exposed to chemicals.

Fasal et al (1968) analyzed deaths from all causes, all

cancer, leukemia and lymphomas in California farm and nonfarm residents between 1959 and 1961. The main findings were as follows. Total mortality was similar in farm and nonfarm residents. Mortality from all cancer was significantly reduced in farm residents with SMRs of 87 for males and 83 for females. Leukemia mortality was not reduced in farm residents. Both male and female farm residents had SMRs of 114, compared to 99 and 100 for male and female farm residents. The mortality experience of farm residents from all lymphomas closely resembled their experience for all cancer with SMRs of 91 for males and 87 for females, although there were distinct differences between the SMRs from lymphosarcoma and reticulosarcoma, Hodgkin's disease and multiple myeloma for all farm residents and between the sexes.

### Leukemia

Mitelman, Nilson and Brandt (1984) reported at the Fourth International Workshop on Chromosomes in Leukemia which studied the relationship between exposure to potential mutagenic carcinogenic agents and karyotypic abnormalities. This prospective collaborative study confirmed previous observations in retrospective studies that clonal chromosomal aberrations are more common in bone marrow cells of patients with ANLL previously occupationally exposed to potentially mutagenic/carcinogenic agents than in nonexposed patients. In addition, the Workshop data demonstrated that the relationship between chromosomal abnormality and occupational exposure is only evident in patients 30 years or older. Among the patients 30 years or older who were exposed to chemicals, a remarkable overrepresentation of the specific karyotypic aberrations - 5 and/or - 7 was observed. Further epidemiologic studies of occupational hazards are needed to define the possible chemical agent(s) associated with these aberrations. Occupational handling of organic solvents may be of special interest. A notably high incidence of the specific translocation t(8;21), was found in the small group of patients who had worked with minerals. A relatively large proportion of

patients with this abnormality also was observed in those occupationally exposed to petroleum products or their combustion residues. Clonal abnormalities other than those specifically recorded were much more common among patients exposed to petroleum products and those who had worked with minerals. It is possible, therefore, that exposure to petroleum products or their combustion residues also may be associated with other specific, but as yet unrecognized, abnormalities as well as t(8;21). Among the patients considered to be exposed to insecticides, clonal abnormalities other than those specifically recorded were common, as well. Most of these patients were farmers, and it is possible that many were exposed to potential hazards other than insecticides, e.g., combustion residues from machinery used in agriculture.

Armstrong (1984), commenting on a study done by McCabe (1984) suggests that more research is needed and should not be purely descriptive. Studies that relate occurrence of leukaemia to individual exposure to chemicals should be carried out. He suggested it would be simple enough to mount a case-control study of leukaemia in northern Queensland, concentrating, among other things, on lifetime occupational history and the chemical exposures experienced in each occupation.

Burmeister (1982) analyzed death certificates of 1675 white, male Iowans over age 30 years who died of leukemia in 1964-1978. Each case was matched to two controls on age (within two years) at death, county of usual residence and year of death. Consideration of usual occupation, as recorded on the death certificate, resulted in an odds ratio for leukemia mortality among farmers of 1.24 ($p < 0.05$). The highest odds ratios for farmers were observed in those born after 1890, those dying after 1970, and those dying at age 65 years or younger. Odds ratios for farmers were also elevated in counties with high soybean and corn production per acre for those born between 1890 and 1900. For those born after 1900, odds ratios for farmers were increased in counties with the greatest numbers of egg-laying chickens and the largest number of acres treated with herbicides. The types of leukemia causing elevated mortalities in Iowa farmers were chronic lymphatic and unspecified lymphatic. Mortality from

unspecified lymphatic leukemia was associated with corn per acre, number of milk cows and number of egg-laying chickens.

Blair and White (1981) studied the risk of leukemia among farmers and dairy farmers in particular with the use of mortality records from Wisconsin, 1968-76. A comparison of occupation as noted on the death certificate for 1,499 cases and a like number of matched controls revealed a slight (odds ratio (OR) = 1.10), but statistically nonsignificant, excess risk of leukemia among farmers. The risk was highest among those born after 1897 (OR = farmers (whether noted on death certificates or identified by county agricultural agents of the Cooperative Extension Programs of the University of Wisconsin) and all farmers alike. The under representation of farmers among controls with smoking-related causes of death, however, may partially account for these findings. Stratification by county of residence showed significantly elevated risks among farmers from counties with heavy dairy production (OR = 1.40) and fertilizer use (OR = 1.41).

Blair and Thomas (1979) studied the risk of leukemia among farmers using records of death certificates from Nebraska, 1957-1974. Comparison of occupation, as recorded on the death certificate, for 1084 leukemia deaths and 2168 deaths from other causes, matched for age at death, year of death, county of residence, race, and sex, revealed an elevated risk of leukemia among farmers (odds ratio = 1.25). The risk was greatest among farmers born after 1900 and dying before age 66 (odds ratio = 1.83). Stratification by county of residence showed a significantly elevated risk for farmers from heavy corn producing counties.

Donham et al (1980) collected data from the Third National Cancer Survey under the auspices of the National Cancer Institute's Surveillance, Epidemiologic and End Results (SEER) Program and used them to perform a descriptive epidemiologic study of leukemia in Iowa. Data were also collected on livestock population patterns in the state, and a survey was performed to

locate cases of lymphosarcoma within the cattle population. Ecologic relationships between human leukemia, livestock populations and bovine lymphosarcoma were investigated. Iowa has higher rates than the national average for human leukemias. The lymphoid leukemias make up the majority of the excess leukemias. Excessive acute lymphoid leukemia (ALL) is seen in the ages under 20 years and over 60 years. The excess ALL is in males living in rural counties. There is no sex difference for chronic lymphoid leukemia (CLL), but there is a slight urban-rural differential. There is a high positive correlation between ALL in males and cattle density. This relationship is greater for dairy cattle than for beef cattle. There is an additional positive relationship between counties with excessive ALL and the presence of dairy herds affected with bovine lymphosarcoma.

Linos et al (1980) reported that between 1955 and 1974, 138 cases of leukaemia occurred in residents of Olmsted County, Minnesota. Each case was compared with 2 control subjects matched for age, sex, and residence with regard to their occupational and chemical exposures before the diagnosis of leukaemia. Farming and health-related occupations have been previously implicated in the development of leukaemia and occurred frequently enough in their group of patients and control subjects to permit analysis. Neither of these 2 occupations occurred more frequently in cases than in control subjects.

Linos et al (1978) extended a study of the period 1935-1964 and determined the incidence rates of leukemia in Olmsted County during the decade 1965-1974. In this decade, the overall crude annual incidence rate was 9.5 per 100,000. The ratio of males to females was 2.4 to 1; and the incidence rate was significantly higher among males than among females, especially in the older age groups. Adjusted for age and sex, the mean annual incidence rate among males (17.3) was significantly higher than rates reported previously from other areas (ranging from 10.7 to 13); and it had increased significantly during the 40 years 1935-1974 in Olmsted County. The increase was most prominent in males aged 50 and over, and was detectable only in the subgroup with acute myelocytic leukemia. The observed number of farmers (8) was

significantly higher than expected (2.8).

Kwiatkowski (1972) studied the effect of fertilization of soil with potassium salts on territorial distribution of leukemias and malignant tumors in the rural population of the Sandomierz county in the years 1957-1966. In the population of 71.3 thousands, 34 cases of leukemia (morbidity rate 3.36 per 100,000 yearly) occurred. The most frequent form of leukemia was acute leukemia, and the most frequent malignant tumor was carcinoma of the stomach. Gastric carcinoma and other tumors were most frequent in areas where soils were fertilized extensively with potassium salts, and least frequent in areas where fertilization of this type was seldom employed. Leukemias were not similarly correlated lymphomas.

Milham (1971) analyzed deaths from leukemia-lymphoma group cancers and occupation as stated on death certificates and revealed a statistically significant association between farming occupations and death from leukemia and multiple myeloma. No such association was seen for Hodgkin's disease, reticulum cell sarcoma, or other lymphomas. The leukemia-forming association was strongest in men under age 60 with lymphatic and acute types of leukemia. Poultry farmers showed the highest proportionate case excess in the leukemia study. These findings are consistent with the hypothesis that agricultural environments contain agents which may cause leukemia.

Priester et al (1970) reported a prospective study of cancer among individuals living on dairy farms where bovine leukosis had occurred and had been histologically confirmed. Among the 98 reporting farms with leukosis there were 4108 person-years at risk as compared with 7968 person-years at risk on the 212 reporting control farms. The survey data were used to obtain expected mortality from all causes, including cancer and leukemia-lymphoma, adjusted for age and sex, for the case and control series. There were no statistically significant differences in observed-versus-expected values. In a study of this magnitude there is a 95% probablility of detecting a 2.4-fold or greater

increase in human cancer mortality associated with bovine leukosis. The data for human leukemia-lymphoma was too sparse to permit estimation of an upper limit on risk. However, the single death in this category did occur in the control rather than the leukosis series.

Khokhlova and Rakhmanin (1970) presented the results of a comparative study of the prevalence of human and cattle leucoses within the territories of the Latvian and Estonian Republics of the USSR. The investigations performed provide no grounds for the establishment of a unique dependence of human leucoses on those of cattle. However, the data obtained must be treated with utmost care. It is possible that the period covered by the investigation (3-5 years) is insufficient to reveal the probable communications. It is of interest that in the Baltic Republics where the leucosis prevalence in cattle reaches the highest figures in the USSR, the mortality caused by leucoses and other hemoblastoses in rural population approaches, and in some years even slightly exceeds the respective figures for urban population. Due consideration should also be given to such facts as the occurrence, within one year or a short interval of time, of two or three cases of leucosis in human beings at one farm or adjacent farm, these settlements being situated mainly in the vicinity of those collective farms where the cattle are affected by leucosis.

### Hodgkin's Disease

A case study presented by Lemon et al (1966) observed that an 18 year old male with Hodgkin's disease diagnosed 2 years previously, involving lung, cervical and pelvic nodes with right ureteral obstruction, resided on an Iowa farm where he had raised a herd of 50 Holstein dairy cattle since 1956. No outside additions to the tuberculin and Bang's negative herd had been made in the preceding 8 years, which was the family's milk source. In June 1965 peripheral lymphadenopathy to 3.0 cm was noted in 1/2 of the herd, whose hemograms showed absolute (over 5000/mm3) and relative (60-96%) lymphocytosis in 2/3. Biopsies revealed nodal hyperplasia with preservation of peripheral

follicular architecture, and unusual protein crystalloid inclusions in plasma cells by electron microscopy. In January 1966 cow #7 died of bovine leukosis and uremia, with involvement of the right atrium, abomasum, mesenteric nodes and both ureters. Hemograms of the proband's relatives show 40-54% lymphocytes, including some immature cells. A second cousin on a nearby farm also had Hodgkin's disease. Another example of symbiotic association of species providing reservoirs for possible cross-infection may be developed by extension of these studies.

Schwartz et al (1978) observed that a cluster of Hodgkin's disease (HD) cases occurred in a small rural town of 1250 people. Ten cases of HD and three cases of non-Hodgkin's lymphoma were identified within or linked to this town since 1954. This town therefore had an average annual incidence and mortality for HD of 29.3 and 16.7 cases per 100,000 population, respectively. Most cases of HD demonstrated case-contact associations, and a distinct geographic distribution. The data suggested that there was an environmental agent responsible for the elevated rates of HD. One unique aspect of this cluster is that this town had only one industry, a large grain elevator. The cases closely surrounded this elevator. They postulate that residents of the town are subject to chronic immune stimulation from mitogenic substances in this environment. These agents may alter immunity in the residents of this community and predispose them to acquiring HD.

Klinger and Minton (1973) reported that a study of the incidence of Hodgkin's disease in a small rural township in Ohio since 1960 revealed five diagnosed cases, four since 1968 - an attack-rate equivalent to 77 per 100,000, as compared with an expected rate of 4.3 per 100,000. Inquiries among patients, friends, and family members pointed to associations between patients similar to the patterns reported by investigators in Albany, N.Y. This is the first such clustering of Hodgkin's disease to be reported - i.e., clearly a space-time cluster with the added feature of an association-between-cases clustering.

## Non-Hodgkin's Lymphoma

Cantor (1982) conducted a case-control study of non-Hodgkin's lymphoma (NHL) and its subtypes among males using computerized mortality listings from the State of Wisconsin for the years 1968-1976. Age, year of death, race, county of usual residence, marital status, and usual occupation were abstracted for the 774 records of male deaths due to NHL and a matched series of deaths due to other causes. The frequency of farming occupation among NHL cases was compared to the frequency among controls, and odds ratios (OR) were calculated. Farming was more common among cases than among controls (OR = 1.22). The association of NHL with farming occupation was greater among decedents under 65 years of age (OR = 1.7) than among those who were older. The younger decedents were at higher risk of reticulum-cell sarcoma (OR = 2.7) than of other cell types. The strength of the association increased over the 9-year study period. County levels of selected agricultural characteristics were used as surrogate measures of farming exposures in residence counties of farmers and were summarized by factor analysis. Major findings were of elevated risk among younger farmers for reticulum-cell sarcoma in counties high in summary measures of general agricultural activity (OR = 32.), of small grain acreage and acres treated with insecticides (OR = 6.6), and of wheat acreage (OR = 4.4). Given the limitations of the data, further investigation of non-Hodgkin's lymphoma in farmers is warranted.

DeKraay (1978) discusses the possible linkage between lymphomas and water supplies. Some evidence exists which shows increased dieldrin levels in drinking water may relate to lymphomas. In 1975 the Des Moines River water at Ottumwa was analyzed for chlorinated hydrocarbons, namely DDT, dieldrin and atrazine. These compounds were found to be present as residues of farm pesticides. Since Ottumwa drinking water comes from the Des Moines River, the possibility of a cancer increase was considered. In 1974 the American Cancer Society published a survey of malignancies in Iowa from 1969 through 1971. The malignancy showing significant increase in Wapello County, on a

population basis, was lymphoma. An analysis of the lymphoma pattern throughout the state suggests there are more lymphomas in counties along the Des Moines and Nishnabotna rivers than might be expected. At a congressional hearing in 1974, laboratory evidence showed dieldrin was a carcinogen. As a consequence, river water levels of dieldrin have been considered to have a possible relationship with the development of lymphoma. Following the 1974 congressional hearing, dieldrin sales were banned by the FDA. It will be interesting to see if the ban on dieldrin will alter the level of lymphomas in Iowa after 1974. Between 1952 and 1972 110 patients were diagnosed as having either Hodgkin's disease or non-Hodgkin's lymphoma at the Ottumwa Hospital and St. Joseph Hospital. Most were between ages 60 and 80. In most series Hodgkin's disease represents 40% of all lymphomas.

## Multiple Myeloma

Cantor and Blair (1984) conducted a case control study of multiple-myeloma among males with the use of digitized mortality listings for 1968-76 from the State of Wisconsin. Age, year of death, race, county of usual residence, marital status, and usual occupation were available for the 411 male deaths due to multiple myeloma and for a matched series of deaths due to other causes. Farmers were at an elevated risk compared to nonfarmers (odds ratio (OR = 1.4)), with decedents 65 years of age or older having a stronger association (OR = 1.5) than younger farmers (OR = 1.1). County levels of selected agricultural characteristics were used as surrogate measures of exposure. Significantly elevated OR were observed for farmers residing in counties high in chicken inventory (OR = 1.6), fertilizer use (OR = 1.7), and acres treated with insecticides (OR = 1.9). Further investigation of multiple myeloma among farmers is warranted.

Gallagher and Spinelli (1983) reported that in a case-control study of 84 multiple myeloma patients and 168 age and sex-matched controls with tumours at other sites, prior allergies

were associated with an elevated risk of myeloma (RR = 3.1, $P < 0.001$). In addition, more myeloma patients than controls reported prior myxoedema (RR = 50, P = 0.04). History of agricultural work was associated with an elevated risk of myeloma (RR = 2.2, P = 0.01), although no detailed information was available on the type of farming in which the subjects were engaged.

Blattner et al (1980) reported that multiple myeloma (MM) is the most common lymphoreticular neoplasm in non-whites and the third most common in whites, yet little is known about etiologic determinants. Age-adjusted mortality rates for the 54,522 deaths from MM during 1950-69 were correlated by race and sex with demographic, industrial, and agricultural data for 506 United States state economic areas (SEA's). The Far West and North Central geographic regions recorded the highest rates for whites, while low rates were seen in South Central and Midwest regions. For non-whites, mortality was high in the Northeast and Midwest and low in the Southeast and South Central regions. Highly urbanized SEA's and large population centers had the highest rates for both races. Over time (including additional data through 1975) there has been a progressive increase in MM mortality, particularly among non-whites. SEA's with elevated rates were characterized by increased numbers of workers in the printing, rubber, fabricated metal, machinery, and transportation industries for non-whites, and food processing and petroleum industries for white males. No excess was found in agricultural SEA's, contrary to prior reports.

Nakayama et al (1980) reported on a case of multiple myeloma in a 78 year old man and in his 69 year old wife. A predominant clinical feature in both cases was the presence of neuropathy. The marked similarity of the clinical features in these cases, together with the fact that the cases occurred almost simultaneously, suggested the possibility of common etiological factors. Neither patient had a previous history of exposure to radioactive substances or to chemical agents except for benzene hexachloride (BHC), to which both patients had been exposed for 30 years while employed as agricultural workers.

Agu et al (1980) correlated age-adjusted mortality rates for multiple myeloma in Texas State economic area(s) (TSEA) with selected occupations. After control was made for the percentage of population classified as black, the positive association between the age-adjusted mortality rate from multiple myeloma and percentage of the population in each TSEA employed in beauty shops, carpentry, and agricultural industries was significant. The findings emphasized the possible importance of race as a confounding variable in ecologic analyses of environmental and industrial exposures associated with mortality due to multiple myeloma. The data supported previous findings by another investigator of a strong association between farming occupations and death from multiple myeloma.

Linet (1984) reports four suspect exposures shared by a husband and wife who developed the rare, B-cell tumors, chronic lymphocytic leukemia and multiple myeloma. While some investigators hypothesize that the occurrence of these diseases in families is due to immunogenetic causes, they cannot rule out environmental effects since family members often share the same environment for many years. Exposures in this case included paints, insecticides and embalming fluid with the insecticide exposure the heaviest and most suspicious.

## Respiratory Cancer

### Nasal Cancer

Hernberg et al (1983) reported that nasal and sinus paranasal cancers have been associated with several occupational exposures, for example, dust from hardwood, nickel and unspecific agents occurring in the boot and shoe industry. A joint Danish-Finnish-Swedish case-referent investigation was initiated in 1977 to study further the connection between nasal and sinus paranasal cancers and various occupational exposures. All new cases of these cancers were collected from the national cancer registers

(Finland and Sweden) or from hospitals (Denmark). Those still alive who agreed to the interview (N = 167) were individually matched for age and sex with patients with colonic or rectal cancer. A detailed telephone interview was performed according to a standardized procedure. Both the cases and referents thought that their condition was the one under study. The exposures were coded blindly by an experienced industrial hygienist. The results showed associations between nasal or sinus paranasal cancer and exposure to hardwood or mixed wood dust (discordant pairs 14/2); softwood dust alone (13/4); chromium (16/6); nickel (12/5, not significant); welding, flamecutting and soldering (17/6); and lacquers and paints (12/0). Hardwood dust exposure showed a connection with adenocarcinoma. Softwood dust exposure alone was associated with epidermoid and anaplastic carcinomas. No associations were found for a number of exposures, including agricultural chemicals, textile dust, asbestos, quartz dust, organic solvents, and leather work. Possible exposure to formaldehyde was evenly distributed between the cases and referents.

Hardell et al (1982) observed that soft tissue sarcoma and malignant lymphoma have been related to exposure to chlorinated phenoxy acids or chlorophenols as well as exposure to organic solvents and malignant lymphoma. However, colon cancer studied by the same case-referent design did not show any such associations, which helps to rule out alleged systematical bias of the study approach. Further considerations about exposure routes for phenoxy acids and chlorophenols suggested that nasal and nasopharyngeal cancers should be studied. Forty-four cases with nasal cancer and 27 cases with nasopharyngeal cancer were eligible for study during 1970-1979 together with 541 referents, as utilized also in the aforementioned studies. Exposure to phenoxy acids gave a doubled but insignificant risk for the studied cancer types. Exposure to chlorophenols, as present particularly in woodwork, was related to an about sevenfold and significant increase in the risk for both cancer types. In wood-workers without exposure to chlorophenols there was an approximate normal risk, but cabinet makers, even without exposure to chlorophenols, had nearly doubled (but insignificant)

risk of nasal cancer.

Tola et al (1980) studied the role of occupational exposure in the causation of nasal cancer. Occupational exposure histories of 51 patients greater than 35 years with malignant tumors of the nose and paranasal sinuses were collected by questionnaire, with returns by 45 patients and 45 control subjects. No specific exposure was significantly over-represented among the cases. There were no exposures to nickel or chromium; there were a few painters, joiners, farmers, and leisure time carpenters and knitters. The latter appeared to be a risk indicator of nasal cancer in women (perhaps from textile dusts and dyes); also previous nasal trauma appeared to be a risk indicator. No conclusive data were derived from this study, but more sensitive approaches to test, for example, the association of exposure to wood dust with histologically verified adenocarcinoma are being undertaken.

## Laryngeal Cancer

Flanders et al (1984) conducted a case-control study to identify employment-related risk factors for laryngeal cancer. Richmond County, Georgia, and the contiguous counties were chosen as the study area because the 1950-1969 laryngeal cancer mortality rate for white males in Richmond County was almost double the corresponding rate for the entire United States, and because a large proportion of the working population was employed in industries for which excess risk among workers had been reported. All persons with newly diagnosed squamous cell carcinoma of the larynx treated in the area hospitals were identified. Potential controls were selected from patients admitted to these hospitals during the same time period as the cases, excluding those patients admitted for cancer, lung disease, or employment-related disease. Eighty-five control subjects were individually matched to 42 cases for sex, age, area of residence, and smoking and alcohol-drinking history. From lifetime employment histories, laryngeal cancer rate ratios were

estimated comparing the incidence rate among subjects who had ever worked in an occupation with the incidence rate among subjects who had never worked in that occupation. Among the 10 occupations in which at least 15 subjects had worked, the authors found rate ratio estimates above 3.0 for farmers, textile processors who separated, filtered or dried textile fibers, and for all laborers and maintenance personnel.

Chodynicki et al (1980) studied epidemiological characteristics of cancer and precancerous changes of the larynx in 100 patients. Precancerous changes (pachyderma, vocal cord polyp, papilloma, and chronic laryngitis) were found in 49 patients (Group I: 43 men and 6 women, 20-79 years old) and laryngeal carcinoma in 51 (Group II: 49 men and 2 women, 30-79 years old). Thirty-three patients in Group I and 21 in Group II were blue-collar workers, 10 patients in Group I and 12 in Group II were white-collar workers, and 3 patients in Group I and 18 in Group II were farm workers. The irritating factors included smoke in 12 cases in Group I and 13 cases in Group II, dust in 20 and 11 cases, respectively, pesticides in 9 and 18 cases, acids in 6 and 24 cases, bases in 1 and 2 cases, tar in 1 and 3 cases, asphalt in 0 and 2 cases, and other in 7 and 4 cases. Forty-one of the 49 patients in Group I and 51/51 in Group II were cigarette smokers. Six patients in Group I and 3 in Group II consumed alcohol several times a week, 26 in Group I and 35 in Group II consumed alcohol several times a month, and 14 patients in Group I and 8 in Group II consumed alcohol several times a year. The fruit and vegetable consumption was higher in Group I than in Group II. Cancer in the immediate blood relatives was found in 10/51 patients in Group II. The findings indicate that the risk factors of laryngeal carcinoma included smoking, alcohol consumption, occupational risk factors, diet poor in fruits and vegetables, and a family history of cancer.

Lung Cancer

Barthel (1981) investigated the cancer morbidity in a large group of male German agricultural workers exposed to pesticides

through a retrospective cohort study. A total of 169 malignant tumors were diagnosed in 1658 men who began to work with pesticides between 1958 and 1972 and who continued this type of activity for at least 5 years. The SMR (standardized mortality ratio) of 2.0 for lung cancer morbidity (mortality) in these pesticide-exposed subjects was significantly higher than that for the general male population of the German Democratic Republic. A positive correlation between the duration of employment and the mortality due to lung cancer (mainly undifferentiated and small-cell carcinomas) suggested a dose-effect relation. The smoking habits of the exposed men did not differ from those of the general male population of the German Democratic Republic. Because the subjects had been exposed to many different substances, the study does not permit any conclusions to be drawn in respect to the carcinogenicity of individual pesticides. The increased mortality due to lung cancer is presumably the result of an additive effect of different pesticide ingredients or of by-products whose carcinogenic effect has been definitely or tentatively established through experimental or epidemiologic studies (e.g., arsenic, asbestos, chlorinated dibenzodioxins, DD1). The results of the present investigation emphasize the need for effective measures to protect workers during occupational contact with pesticides.

Vianna et al (1981) reported on a study of malignant mesothelioma in New York State, excluding New York City. It suggests that there was no increase in the incidence of disease from 1973 through 1978. The highest rates for this tumor were observed in six rural counties, and farmers, talc miners, and paper workers were the most common occupations involved. Certain other highly industrialized counties in close proximity to major waterways also had higher incidence rates than the State as a whole.

Mosbech (1980) presented mortality data for diseases of the respiratory tract in the age bracket 15-64 years in Denmark for the period 1970-1975. For men, the standard mortality ratio for malignant tumors of the respiratory organs was 116 (i.e., higher

than the expected value of 100%) in urban areas, 72% in rural areas, and 46% among agricultural workers. The standard mortality ratio is significantly lower than 100% in the rural areas and among agricultural workers at the 95% level. The standard mortality ratio for malignant tumors of the respiratory organs was 69% in rural areas and 100% in urban areas for married women, and 70% in rural areas and 146% in urban areas for single women. The standard mortality ratio for the married and single women in rural areas is significantly lower than the expected mortality at the 95% level, while it is increased significantly at the 95% level in the single women in urban areas. Differences in smoking habits between men and women and between urban and rural areas may partly explain the differences in the standard mortality ratios.

## Soft Tissue Sarcoma

Balarajan and Acheson (1984) used the National Cancer Register maintained by the Office of Population Censuses and Surveys (OPCS) to investigate the relative risks of soft tissue sarcomas among farmers, agricultural workers, and related occupational groups. The relative risk for the group as a whole was 1.15 (95% confidence limits 0.83-1.59). One of the four subgroups (which comprises farmers, farm managers, and market gardeners) experienced a relative risk of 1.7 which just achieves significance at the 5% level (95% confidence limits 1.00-2.88). The risks in the other three subgroups were respectively 1.0 (agricultural workers, 003), 0.7 (gardeners and groundsmen, 005), and 1.0 (foresters and woodmen, 006). No attempt has been made in this study to determine exposure to phenoxy herbicides in cases or controls.

Eriksson et al (1981) observed several patients with soft-tissue sarcomas and previous exposure to phenoxy acids. This clinical observation resulted in a case-referent (case-control) study being undertaken which showed that exposure to phenoxy acids or chlorophenols, which are chemically related gave a

roughly six-fold increase in the risk for this type of tumour. A further case-referent study of soft-tissue sarcomas has now been performed to confirm these earlier findings and also to obtain further information on the effects of different phenoxy acids. This new investigation gave an increase of the same magnitude in the risk for soft-tissue sarcomas after exposure to phenoxy acids or chlorophenols, but this risk related also to exposure to phenoxy acids free from impurities, such as polychlorinated dibenzodioxins and dibenzofurans.

Hardell and Sandstrom (1979) described a number of patients with soft-tissue sarcomas and previous exposure to phenoxyacetic acids. Following from these observations a matched case-control study was made. Exposure to chlorophenols was also included in this study. The results showed that exposure to phenoxyacetic acids or chlorophenols gave an approximately 6-fold increase in the risk for this type of tumour. It was not possible to determine, however, whether the carcinogenic effect was exerted by these compounds or by impurities such as chlorinated dibenzodioxins and dibenzofurans that in almost all cases were part of the commercial preparations.

Moses and Selikoff (1981) reported as part of their continuing investigation of long-term health effects of exposure to dioxin, that they have become aware of another worker with soft tissue sarcoma employed at the Monsanto Chemical Company at a time when trichlorophenol and 2,4,5-T were being manufactured and TCDD is known to have been present as a contaminant. He died in 1980 at the age of 58 of a retroperitoneal neurogenic sarcoma (malignant schwannoma). He had worked for the company for 32 years, retiring in 1975. During their examination in 1979 he reported, in a detailed occupational history, that while he did not work in the production of trichlorophenol or 2,4,5-T, he had had potential exposure as a result of his work as a truck driver, hauler, and maintenance worker. He had never had chloracne. Unlike the other four reported cases he had never smoked. His first exposure would have been in 1948 or 1949.

Ott et al (1980) examined the mortality experience of 204

persons exposed to 2,4,5-T during its manufacture from 1950 to 1971. Length of employment in job assignments within the 2,4,5-T process area ranged from less than one year to a maximum of approximately ten years. Efforts to minimize 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) contamination of the product resulted in nondetectable concentrations using a method of detection developed in 1966 that was sensitive to 1 part per million. Within the scope of this mortality survey, no adverse effects were observed with respect to occupational exposure to 2,4,5-T or its feedstock, 2,4,5-trichlorophenol.

Cook et al (1980) describe the mortality experience of a cohort of 61 males involved in a 1964 chloracne incident. Presumably as a result of skin absorption of the process contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin), 49 of these trichlorophenol production workers developed the skin condition. Within the limitations posed by cohort size and length of follow-up TCDD does not appear to have adversely affected mortality experience. Overall, four deaths occurred and 7.8 were expected. Of these, one death was due to cardiovascular disease (3.8 expected) and three deaths were attributed to cancer (1.6 expected). None of the findings were statistically significant at = 0.05.

Zack and Suskind (1980) conducted a standardized mortality analysis on workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident at the Monsanto Company plant in Nitro, West Virginia. One hundred and twenty-one workers who developed chloracne resulting from this accident on March 8, 1949, were selected for study. Follow-up of this group was 100% complete. The standardized mortality ratio for all causes of death was shown to be 0.69, with 32 deaths observed and 46.41 expected. For the categories of malignant neoplasms and circulatory diseases, the standardized mortality ratios were 1.00 and 0.68 respectively. Because of the small size of the cohort and the relatively small number of deaths observed, the results of this study cannot be considered conclusive. However, it is important that no apparent excess in total mortality or in deaths

from malignant neoplasms or diseases of the circulatory system was observed in a group of workers with a high peak exposure to tetrachlorodibenzodioxin who were followed over a period of nearly 30 years. The results of this study will be incorporated with those of a larger study which will include plant workers exposed in the course of 2,4,5-trichlorophenoxyacetic acid production during the period 1948 to 1969.

Honchar and Halperin (1981) reviewed reports of four exposed cohorts studied by epidemiologists from Dow Chemical U.S.A. and the Monsanto Company. Of the 105 deaths reported in the four cohorts 3(2.9%) were due to soft tissue sarcoma. In rough comparison, for 1975 only 0.07% of deaths in U.S. males aged 20-84 years were due to soft tissue sarcoma. The workers from the four U.S. cohorts were exposed either to the phenoxy herbicide 2,4,5-trichlorophenoxyacetic acid or to 2,4,5-trichlorophenol (TCP), a feedstock for 2,4,5-T. Both 2,4,5-T and TCP are contaminated with the toxic dioxin isomer 2,3,7,8,-tetrachlorodibenzo-p-dioxin which has been found to be carcinogenic in laboratory animals. None of the four cohorts individually resulted in a reported excess risk for soft tissue sarcoma. When combined, however, the three cases from the four cohorts suggest a common pattern. This finding supports the concept of combining small cohorts of workers with a common occupational exposure for analyses. Such an effort to assemble an exposure registry of all people in the U.S. who have worked at the synthesis of 2,4,5-T is underway at the National Institute for Occupational Safety and Health. The mortality experience of the combined cohort will be analysed retrospectively and followed up prospectively. This approach will provide greater statistical power than would be available for any subgroup of the registry analysed alone.

Milham (1982) updated an occupational mortality study which sheds further light on the phenoxy herbicide cancer controversy. Only farmers NOS (not otherwise specified) have a significant excess of soft tissue sarcoma, but the total proportional mortality rate (PMR) for these occupations is not significantly increased. Similarly, papermakers have a significant excess of

Hodgkin's disease while the PMR for Hodgkin's disease in these occupations is only 102. Of the 15 occupations (of 218) with the highest PMRs for soft tissue sarcomas, none have an obvious exposure to the phenoxy herbicides or chlorophenols. The dry cleaners, printers, and mechanics have solvent exposure. The mortality patterns seen here do not offer convincing support for the phenoxy herbicide and chlorophenol link to soft tissue sarcomas, Hodgkin's disease, and non-Hodgkin's lymphomas.

## Gastrointestinal Cancer

### Esophageal Cancer

Muir (1981) looked at epidemiology of cancer of the esophagus in France and in the world. In England and in Wales, the barmen and the agricultural workers face higher mortality from esophageal cancer. The slightly lesser risk registered amongst the agricultural workers of the Cote d'Or was somewhat unexpected. However, this analysis has a very relative bearing, in the fact that the precise determination of the profession was only able to be ascertained in 40% of the cases; given that the average age at the time of diagnosis was more than 64 amongst the men, this is not surprising.

Faivre et al (1981) established a register of digestive cancer cases in the French department of the Cote-d'Or (455,727 inhabitants) to study morbidity of esophageal cancer. The crude annual incidence rate was 16.2/10,000 for males and 1.0/100,000 for females. Corresponding rates standardized for age were 12.9 and 0.5 respectively. Cancer of the esophagus represents 13 % of digestive cancers in males and 1 % in females. Esophageal cancer risk is lower among the highest socio-economic strata and agricultural workers (relative risk = 0.38, $p < 0.05$). The patients were scattered throughout the Cote-d'Or with no higher incidence in any particular region. The risk of an associated upper respiratory tract tumor is high (17 % 100). Only 11 % of the patients underwent curative surgery, while 51 % were

referred for radiotherapy alone. The three year actuarial survival rate was 6.7 %.

de Jong et al (1974) reported that an analysis of a hospital-based case-control study of esophageal cancer among Singapore Chinese (composed of Cantonese, Hokkien, Teochew and other dialect groups) revealed the following statistically significant risk factors for both sexes: (1) belonging to either Hokkien or Teochew dialect groups; (2) the consumption of beverages at temperatures stated subjectively to be "burning hot" prior to illness; and (3) the smoking of Chinese cigarettes. Additional risk factors for males were birth in China and the consumption of Samsu (Chinese wine). Consumption of bread, potatoes and bananas was reported at significantly lower levels in male esophagus cancer patients than in controls. Esophageal cancer was less common in males who had attended school for more than 8 years. Multivariate analysis (examination of the joint influence of selected variables) confirmed the strong effects of dialect group and beverage temperature for both sexes. For females the smoking of Chinese cigarettes remained a risk factor, for males the consumption of Samsu. The smoking of western-type cigarettes and the consumption of strong liquors were not significantly related for either sex. These findings suggested that esophageal cancer is more likely to occur among "traditional" Chinese who maintain dietary patterns which include Samsu and the drinking of beverages at hot temperatures, but avoid the bland foodstuffs (bread, potatoes and bananas) not native to their culture. The greater risk in Teochew and Hokkien may be due in part to the consumption of a greater number of beverages at "burning hot" temperatures compared with Cantonese and other dialect groups. However, these differences are based on subjective impressions which need to be verified by actual measurements of the temperature of drinks consumed by members of these population groups.

Stomach Cancer

Armijo et al (1981) reported the results of a case-control study of stomach cancer carried out with the collaboration of 7 participating hospitals in Santiago, Chile. Patients attending gastroscopy clinics were interviewed before or after gastroscopy. The diagnosis was unknown to either the patient or the interviewer at the time of interview. 360 stomach cancer cases were subsequently matched to non-cancer patients selected from the pool interviewed at the same time as the cases. Study findings show: 1) longer-term residence in high-risk areas in early life by cases than controls; 2) an association between stomach cancer and a prior occupation in agriculture. In a subgroup of 98 cases for whom histologic classification was available, the association with residence in early life in a high-risk area was seen only for cases with intestinal-type stomach cancer.

Duris et al (1981) studied precancerous conditions and cancer of the stomach in 4,159 patients subjected to gastroscopy. The histological diagnosis was that of gastric polyps in 112 patients, atrophic gastritis with intestinal metaplasia (AGIM) in 190, and gastric cancer in 103, including intramucosal carcinoma in 9. All patients with gastric carcinomas were in the age bracket 20-90 years, and the frequency was higher among men than among women in all age groups. The incidence of AGIM was higher among women than among men in the age group 40-70 years, especially in the age group 50-60 years. Gastric cancer was found to occur at a significantly higher age among agricultural workers than in the other occupational groups.

Amadori et al (1980) carried out an epidemiological research on gastric cancer mortality rates in the town of Forli. The results are significant as regards the relation between the urban and rural areas, and show a higher risk for gastric cancer in the rural area. Salivary nitrite measurement in 92 farm workers showed particularly high values (over 30 ppmm in 4 individuals). Analysis of histological findings in biopsies performed during endoscopy in 46 persons of the group studied showed a great number of CAG and CAG + IM in asymptomatic individuals.

In a review of exogenous factors in the epidemiology of gastric carcinoma, Pfeiffer (1979) observed that an increased risk of gastric carcinoma (GC) is associated with such exogenous factors as general environment, diet, occupation, smoking and drinking. Data show that many carcinogens, including chemical agents may initiate gastric carcinogenesis, that pathogenesis is very slow to develop, that diffuse and intestinal types of gastric cancers may have different causal factors, and that chronic atrophic gastritis and intestinal metaplasia are closely associated with gastric cancer. Among occupations implicated are rubber work, farming, and fishing industry. Ethnic differences do not appear to account for the variation in gastric carcinoma mortality.

Zaldivar and Witterstrand (1975) presented further evidence of a positive correlation between exposure to nitrate fertilizers ($NaNO_3$ and $KNO_3$) and gastric cancer death rates by using stable death rates for stomach cancer in the 25 Chilean provinces (mean age-adjusted death rates per 100,000 for 1960, 1962 and 1964), relating this variable with sodium nitrate exposure as well as with exposure to nitrates ($NaNO_3$ and $KNO_3$). The regression of death rates on the general population exposure to sodium nitrate showed a highly significant association ($p < 0.00005$). The regression of death rate on the farm workers exposure to sodium nitrate exhibited a significant association ($p < 0.0001$). The regression equation is $y = 35.87 + 154.0\ x$, where y is mean death rate and x is metric tons of sodium nitrate per farm worker. The regression of mortality rates on the farm worker exposure to nitrates showed again a significant association ($p < 0.0003$). As previously postulated 8-10, the most probable expalanation for this relationship is the nitrosamine formation in vivo. Chilean farm workers would be exposed to dietary nitrates and nitrites, primarily from water supplies. The general population of Chile is exposed to nitrates and nitrites from food additives. The correlation presented in this communication is apparently not an artefact nor a causal association but an indirect association, i.e., a factor (nitrate fertilizer) and a disease (gastric cancer) are associated only because both are related to some

common underlying condition or process (nitrosamine formation). However, at present we cannot entirely rule out a carcinogenic or co-carcinogenic effect of dietary nitrate per se on the human stomach.

Zaldivar and Robinson (1973) made a statistical analysis of the relative contributions of exposure to fertilizer, rainfall and latitude to the variability of gastric cancer mortality rates in the Chilean Provinces. The relative contributions of these independent variables to variability in the death rates were evaluated by multivariate analysis. The method used was stepwise multiple regression. Results indicated that the major factor studied influencing stomach cancer mortality rates for the Chileans is the exposure to sodium nitrate used as fertilizer. When the mortality rates by Provinces were regressed on the exposure to sodium nitrate, a statistically significant association ($p < 0.02$) was found. Associations between gastric cancer death rates on the one hand and proportions of farmers and farmer exposure to sodium nitrate on the other hand, indicate that farmer deaths are influencing the death rates by provinces. Male workers in actual contact with the soil, such as farmers (31.2%) and miners (18.7%), accounted for 49.4% of all male deaths from stomach cancer, that is 837 cases.

Armijo and Coulson (1975) observed that Chile ranks second in the world regarding age-adjusted mortality rates from stomach cancer. Analysis of death rates along its 25 provinces for a 15-year period (1957-1971) shows a peculiar geographic pattern of high and low-risk areas. Three agricultural provinces (Maule, Linares and Nuble, located south of Santiago), population 460,000, show a median rate of 50-1 per 100,000. In contrast, both extremes of the country, distant some 3,000 miles from one another, carry less than one-half the risk. Data showing the use of nitrates throughout the country were collected for the period 1945-1972. A high correlation has been found between death rates and cumulative per capita exposure to nitrogen fertilizers. Controlling for confounding socio-economic variables, estimated by housing and infant mortality rates, the correlation holds at a significant level. A negative correlation between stomach cancer

and infant mortality rates, low correlation with housing rating, and a negative correlation with lung and cervical cancer deaths were also found. The latter reinforces the lack of association with socio-economic conditions. Other major sites show a completely different pattern. The epidemiological evidence presented agrees with biochemical findings on the synthesis of nitrosamines.

Mastroangelo et al (1981) describes the geographical distribution of gastric cancer (GC) by age and sex in the Unita Sanitaria Locale (health authority area) of Bassano, situated in the north-eastern part of Italy (population 115,380 in 1971). The geographic distribution of observed and expected cases of GC in the 20 towns of district fails to indicate a definite relationship with the characteristic of economic development, e.g. percent of employed in industry or agriculture, in each town.

Armijo et al (1981) determined nitrate levels in urine and nitrite levels in saliva in school children 11-13 years of age in 2 areas of high stomach cancer mortality located in central Chile and in 2 areas of low stomach cancer mortality located at the extremes of Chile. Levels of both nitrates and nitrites were concurrently determined in selected vegetables obtained in these 4 study areas. Levels of nitrates were significantly higher in the urine of schoolchildren and in vegetables obtained from the northern low-risk area. Levels of nitrites were similar in saliva specimens from all 4 areas, but levels in vegetables were inconsistent. These results are apparently incompatible with the hypothesis of a high nitrate intake in areas of high stomach cancer incidence compared to areas of low incidence. This paradoxical finding suggests that cofactors may be involved in the pathopoiesis of stomach cancer that promote or inhibit the transformation of dietary nitrates to nitrosamines. The soil in the high-risk areas is primarily of volcanic origin, which is reported to be low in levels of selenium. On the other hand, residents of Antofagasta, the northern low-risk area, are known to be exposed to high levels of arsenic. It is possible that the

diet of residents of the high-incidence area which may be deficient in selenium may enhance promotion of nitrates to nitrosamines as has been reported in the literature, or conversely, that high levels of arsenic or other factors in the diet of individuals in Antofagasta may play a protective role. Other factors may be responsible for the low rate observed in the southern low-risk area.

## Liver Cancer

Falk et al (1981) studied the occurrence of hepatic angiosarcoma (HAS) in the United States for the period 1964-1974. Death certificates were reviewed in 22,432 cases of death due to liver tumors. Based on examination of medical records and pathological specimens, 168 cases of HAS were confirmed. Of cases identified as HAS on death certificates, only 42% were confirmed as HAS by other evidence; 50% were confirmed as not HAS. Only 23% of confirmed cases of HAS would have been identified by a search of death certificates alone. Inadequacies in epidemiological studies are indicated. Of 127 men with HAS, 12 had been exposed to vinyl chloride (VC), 15 to Thorotrast (TT), 4 to inorganic arsenic (As), and 3 to androgenic-anabolic steroids (AAS); 93 cases were classified as idiopathic. Of 41 women with HAS, 5 had been exposed to TT, 2 to As, and 1 to AAS; 33 cases were classified as idiopathic. The mortality rate for HAS was 0.75 cases/10(7) population/yr. The mortality rate was apparently higher in industrialized areas of the Northeast and Midwest and lower in farming states and the South; differences in rates for different areas may have been due to reporting methods rather than to actual differences in occurrence. Four agents have been identified as probable causative factors in HAS, but 75% of cases are of uncertain etiology.

Falk et al (1981) conducted an epidemiological study to provide additional evidence for arsenic being one cause of hepatic angiosarcoma (HAS). Four male farmers known to have used Paris green or other unspecified arsenicals for long periods were 68-79 years old at death from HAS. Two other confirmed

cases with deaths prior to 1964 also involved males aged 42 and 50 years with histories of 6 and less than 15 years, respectively. The results were taken as supportive of a 1957 report involving autopsies on German vineyards, some dying from HAS and all having both used arsenical insecticides and regularly imbibed a beverage made from the grape skins.

Stemhagen et al (1983) conducted a retrospective case-control study to identify risk factors associated with primary liver cancer in New Jersey, with particular focus on agricultural occupations and pesticide exposures. Hospital record room, tumor registry, and death certificate searches for the diagnosis of primary liver cancer resulted in identification of 959 cases of which 335 were subsequently confirmed. Interviews were completed for 265 persons with liver cancer diagnosed between January 1, 1975 and March 1, 1980 and for 530 matched controls; 96% of all interviews were conducted with family members of deceased or incompetent study subjects. Analyses of employment in agricultural occupations identified male farm laborers as having an odds ratio of 1.89 (95% confidence interval (Cl) 1.19 - 3.00). An estimated relative risk of 3.20 (Cl 1.11-9.21) was found for males engaged in winemaking. Among nonagricultural occupations, elevated risks were found for males working as bartenders and those employed in eating and drinking places, laundries and dry cleaning services, and gasoline service stations. An elevated risk of liver cancer was also associated with females employed as cleaning service workers. Hepatitis and cirrhosis could not be evaluated as risk factors in this study. Dose-response trends by level of alcohol consumption were found for both males and females.

Pancreatic Cancer

Gold and Diener (1981) reported a case-control study begun in Baltimore in 1978 to investigate factors associated with PC (pancreatic cancer). Over 170 case-neighborhood control pairs have been interviewed. Analysis of the first 107 pairs suggests

that dietary carcinogens may be important. An increased risk was found for living on a farm and having farm animals and for low income (OR equals 3.8). These preliminary findings suggest that dietary factors may be involved in the etiology of PC.

Colo-rectal Cancer

Abu-Zeid et al (1981) completed a study of 197 pairs of all confirmed cases of cancer of colon and rectum and their non-cancer controls (matched for age, sex, race, residence and hospital) admittted during the two years to two hospitals in Winnipeg. A significantly increased risk of colon cancer and rectum was associated with living on a farm, history of appendectomy, and long history of constipation.

Pratt et al (1977) presented results of a study of colorectal carcinoma in adolescents and implications regarding etiology. Between October, 1974 and December, 1976, 13 adolescent patients with far-advanced, poorly differentiated colorectal carcinoma had been referred to a pediatric cancer center. All patients received chemotherapy with vincristine, methyl-CCNU and 5-fluorouracil. Five of 13 patients are living, one of whom remains disease-free after 12 months of chemotherapy. Four of the patients were from urban areas and nine from rural areas. One of four from urban areas had intimate exposure to chemicals used in the production of cotton and soy beans. Eight of nine patients from rural areas also had exposure to farm or agricultural chemicals, and three of these patients were intimately involved with the spraying operations. Suggestions regarding etiology and causative factors for the development of carcinoma of the colon in adults have previously been advanced. Results of these studies suggest that alternate etïologies must be suggested for adolescent colorectal carcinoma.

<u>Reproductive</u> <u>Cancer</u>

Testicular Cancer

Brown and Pottern (1984) looked at data available from a large case-control interview study of testicular cancer in young men. Their study population consisted of 271 testicular cancer cases and 259 other-cancer controls aged 18-42 diagnosed between Jan. 1, 1976 and June 30, 1981, and referred to one of three medical centres in the Washington, DC, area. Study subjects were interviewed personally if they were in the hospital or by telephone if they were not currently being seen in the hospital. Information on all jobs held for six months or longer was collected. Odds ratios were calculated as measures of an association of testicular cancer with ever and current employment in farming and agriculture and with type of childhood residence. No increase in testicular cancer risk was seen for either ever or current farming. The results for agriculture were similar. To see if a childhood spent on a farm was a risk factor for testicular cancer, usual type of childhood residence was examined. The odds ratio was not increased for study subjects who had spent most of their childhood in a rural (farm or small town) rather than an urban area. Controlling for ever farming did not affect the risks (OR = 0.8, confidence limits = 0.5-1.1). When the analyses were redone after removal of 37 controls with leukemia and connective tissue cancer (cancers thought to be associated with farming), no substantial differences in the odds ratios were found.

McDowell and Balarajan (1984) undertook a death certificate case-control study of testicular cancer. The cases were all 1384 deaths in males aged 15 over from testicular cancer in England and Wales for six years (1973-75 and 1978-80). Controls were randomly selected from male deaths from all other cancer sites, with matching by age to within 5 years and with one control per case, 42 cases and 27 controls were recorded as being engaged in farming as their last occupation (relative risk (RR) 1.57; 95% confidence limits 0.94-2.64). Almost all the excess risk for the farming occupations can be ascribed to men recorded as farmers (30 cases, 16 controls; RR = 1.89, confidence limits 0.99-3.60) as opposed to those recorded as farmworkers (12 cases, 11

controls). Their study is being extended to cover 10 years, to investigate further this and some other suggestions of associations between occupation and testicular cancer.

Jensen et al (1984) investigated Denmark's high testis cancer incidence and the high proportion of its population who are in agriculture. Although routine statistics showed that the testis cancer incidence was slightly higher in urban than in rural areas and has been so since 1943, they did a more specific analysis of the information in the Cancer Registry. Occupation at the time of cancer diagnosis has been notified to the registry since its start in 1942. For the 3-year period of 1979-81 they calculated the proportions of 15-69-year-old persons with testis cancer with jobs in farming, gardening, forestry, fishing, and other specified occupations. The cases were divided into those with germ cell tumours and those with other and unspecified testicular cancers. All other malignant neoplasms among males in the same age-groups were selected as controls, except for tobacco-related cancers. All other malignant neoplasms among males in the same age-groups were selected as controls, except for tobacco-related cancers of the lung, bladder, and upper respiratory/digestive tract. 174 cases of germ cell cancer of the testis, 18 cases of other and unspecified testis cancers, and 3221 controls were available for analysis. The age adjusted odds ratio of germ cell tumour development among farmers compared with other specified occupations is 0.97 (95% confidence limits; 0.56 - 1.68; $x^2$ for heterogeneity 5.41, 10 DF, $p = 0.86$). When farming, forestry, gardening, and fishing are considered together a relative risk of 1.00 emerges (95% confidence limites; 0.61 - 1.62; $x^2$ for heterogeneity 6.37, 10 DF, $p = 0.78$). Too few cases of other and unspecified testis cancers are available for meaningful analysis. No indication of an increased risk associated with farming and related activities. It is unlikely that agriculture in Denmark explains the country's high testis cancer incidence.

Mills et al (1984) reported on a hospital-based case-control study, involving review of the medical records of 347 patients with histologically confirmed germ-cell tumours of the testis and

347 randomly selected controls with other disorders, and demonstrated a significant association between this cancer and work in the agricultural industry. The odds ratio for present farming occupation was 6.27 (95% confidence limits 1.83, 21.49; $p < 0.05$). Work in the crude petroleum and natural gas extraction industry also conferred excess risk for this cancer (odds ratio 2.29; CL 1.03, 5.11).

Wong et al (1984) conducted a historical prospective mortality study on 3579 white male workers employed between 1935 and 1976 with potential exposures to brominated compounds including 1,2-dibromo-3-chloropropane (DBCP), Tris (2,3-dibromopropyl) phosphate, polybrominated biphenyls (PBB), various organic and inorganic bromides, and DDT. The vital status as of 31 December 1976 was determined for 3384 (95%) of these workers: 2806 (79%) were still living and 578 (16%) had died. Death certificates were obtained for 541 deaths (94% of all deaths). The mortality experience of the entire cohort and several subcohorts was compared with that of United States white men adjusted for age and calendar time. The comparison statistic was the commonly used standardised mortality ratio (SMR). Historical industrial hygiene data were not available, and the workers were classified by their work areas or departments in order to estimate their potential exposures. Mortality from testicular cancer was significantly higher than expected among those potentially exposed to other organic bromides. The common potential exposure of those who had died of testicular cancer was methyl bromide.

A study was undertaken by Tallerman et al (1974) to examine the incidence of all testicular neoplasms and their two main types, seminoma and teratoma, in urban and rural districts in the Netherlands. The data were obtained from the respective regional cancer registries and analysed. The reasons for choosing these areas were that their medical services are comparable and that their cancer registries are similarly organized and provide accurate incidence data, with histological verification. The incidence of all testicular neoplasms and their two main types (seminoma and teratoma) in the areas described above during the

years 1960-69 inclusive is shown in the table, together with the total and male population and the average annual incidence per million male population. The results show a significantly higher (P <0.001) incidence of all testicular neoplasms, as well as their two main types seminoma and teratoma, in the rural district of Friesland, whereas the incidence of these tumours in both urban communities, as represented by the cities of Rotterdam and the Hague, is similar and considerably lower than in Friesland.

Mikuz et al (1981) investigated 258 testicular tumors registered in the two western provinces of Austria (Tyrol and Vorarlberg) during 1945-1980. The histological slides of all tumors were reviewed and classified according to the revised "British Classification". The most frequent tumors were seminomas (43.4%) and teratomas (38.4%). Like in other investigations also in our material the right side was more commonly affected. The age-adjusted incidence of these tumors revealed a dramatic increase up to 6.3/100,000 in the last year. Districts with high percentage of people employed in agriculture showed low incidence rates.

## Ovarian and Breast Cancer

Donna et al (1984) studied the ovarian cancer risk from herbicide exposure in a hospital-based, case-control study after some of these compounds have been shown to be carcinogenic for animals. This study includes 60 cases of primary mesothelial ovarian tumors and 127 controls with non-ovarian malignancies drawn from the same file and matched by year of diagnosis, age and residence. A positive association (relative risk 4.38) has been found between herbicide exposure and ovarian mesotheliomas.

Melton et al (1980) reported that between 1935 and 1974, 580 new cases of breast cancer were diagnosed among the residents of Rochester, and 187 cases were found among the women living in the remainder of Olmsted County, Minnesota. The age-adjusted incidence of breast cancer was 79.1 per 100,000 person-years

among Rochester women and 56.3 per 100,000 person-years among the rural women, for an urban-rural ratio of 1.40:1. The rural incidence increased more rapidly than did the urban incidence during the period of the study, especially among women 50 years old or older; and the urban-rural ratio seemed to decline with time. No convincing explanation for these changes was found, but migration and increasing urbanisation of rural areas may be important factors. The greater urban incidence and the net migration of rural patients with breast cancer into the urban area explain the higher urban mortality rates for breast cancer.

## Childhood Cancers

Hemminki et al (1981) conducted a case-control retrospective study in Finland from 1959-1975 for parental occupations of children under 15 years with a diagnosed malignancy. Childhood cases were analyzed according to diagnoses (leukemia, brain tumors, and all other malignancies). Occupations found more frequently among mothers of children with cancer than among mothers of controls were farmers' wives (1959-68 series only), bakers, pharmacists, saleswomen, and factory workers of unspecified nature (1969-75 only). The paternal risk occupations appeared to be farming, motor vehicle driving, machine repair, painting, and the work of men who gave an academic degree as their occupation. It was concluded that although in some of these maternal and parental occupations harmful chemical exposure is known to occur, chance correlations cannot be excluded.

Hemminki et al (1980) studied occupational risk factors for childhood cancer, malformations, and spontaneous abortions in Finland using surveillance programs to detect environmental health hazards in population groups. Whether the risk factors for cancer can be used to predict the risk of malformations and spontaneous abortions, and vice versa, was also studied. Children born to fathers in the farming or car driving occupations and to mothers who were bakers appeared to have an elevated risk of contracting cancer. Children born of women in industrial and agricultural occupations are at particular risk of

having malformations or being spontaneously aborted. Those at particular risk of spontaneous abortions appear to be workers in machine shops, or in the plastics and shoe industries. The data suggest that there is no parental occupation group that is a common risk factor for childhood cancer, malformations, and spontaneous abortions.

Infante et al (1978) presented five recently diagnosed cases of neuroblastoma associated with chlordane exposure during prenatal and postnatal development. Three cases of aplastic anemia and three cases of acute leukemia are also reported in association with chlordane formulations. The cases suggesting association between chlordane exposure and neuroblastoma are of interest in view of recent data on the carcinogenicity and mutagenicity of chlordane and heptachlor and in view of data on environmental distributions and body burdens. The cases of aplastic anemia and leukemia are of interest in view of previous literature reports on associations between chlordane and similar chlorinated hydrocarbon pesticides and blood dyscrasias, and in view of reports indicating that some subjects with aplastic anemia convert to leukemia. As previous studies are too limited to allow the development of valid inferences regarding the neoplastic risk of chlordane, there is need for formal epidemiologic study to evaluate health risks associated with chlordane through home exposure and through occupational exposure for termite exterminators, lawn care operators, and for workers in the agricultural setting.

## <u>Excretory System Cancer</u>

### Prostate

In a Canadian study Bako et al (1981) reported that during an investigation of the epidemiologic factors associated with the geographic variation in the incidence of prostatic cancer in Alberta (22.5 to 49.7/100,000 population) it was noticed that agricultural practices, water supply and the amount of cadmium in

the environment differed between high and low-risk areas of the province. In the area called census division 1, in southeastern Alberta, the incidence of prostatic cancer was significantly higher than the average for the province as a whole (by a two-tailed test of significance; $P < 0.05$). Of the total population 68% drank water drawn from the South Saskatchewan River, which is formed by the confluence of the Bow and Old Man rivers. These rivers carry effluent from the industrial complexes around Calgary and run-off water from irrigated lands. Medicine Hat, also in census division 1, which has the highest incidence of prostatic cancer in all of Alberta's cities, depends totally on the South Saskatchewan River for its water supply. Census division 3, in southwestern Alberta, also had an incidence of prostatic cancer that was significantly higher than average. Most of its communities depend on water from rivers that traverse irrigated land and carry effluents from the upstream industries that grew rapidly during the 1960s. In contrast, in census divisions 10 and 12, in east-central and northeastern Alberta, the incidence of prostatic cancer was significantly lower than average. In these regions irrigation agriculture is not practised and only a very small proportion of the population drinks water from either the North Saskatchewan River or the Athabasca River. The industrial effluents and run-off water from agricultural land released into rivers contain various concentrations of cadmium. In addition, many fertilizers are derived from phosphate rock containing a significant amount of cadmium, which is readily taken up by soil and plants. Persons living in cadmium-rich environments can expect to have a high accumulation of this element in their system.

Van Shepen et al (1983) observed that the Mortality Atlas of Canada revealed an unusual clustering of census divisions of high risk of prostatic cancer in rural Manitoba. They undertook a case-control study to determine if the high prostatic cancer mortality in Manitoba was related to this occupation. Cases were the 389 deaths from 1966 to 1976 inclusive among men less than 75 years of age who were usual residents of Manitoba and for whom the underlying cause of death was prostatic cancer. For each case, a "control" death was selected from deaths among Manitoba

residents due to any cause except cancer of the lip, prostate, brain or hematopoietic system, motor vehicle accidents and respiratory or genitourinary diseases. The latter cause of death was excluded to eliminate possible early undiagnosed cases or precursors of prostatic cancer; the former conditions were excluded because other studies have shown farmers to be at high risk. Each control was randomly selected from sub groups of deaths matched by sex, year of death and age at death (± 2 years). Death certificates were examined to retrieve information on usual lifetime occupation and occupations were coded using the 1971 Census of Canada Occupational Classification Manual. Statistical analysis was based on matched-pairs. Although elevated, the odds ratio (1.28) for men in farming and related occupations was not statistically significant. The only statistically significant odds ratio was that for men in construction for whom the risk of prostatic cancer death was low (O.R. = 0.45). Odds ratios for men less than 65 years of age and for older men, respectively, were 1.31 and 1.27 for farming and 0.38 and 0.48 for construction occupations (the latter two ratios were statistically significant). There were weak positive but statistically insignificant correlations betwen prostatic cancer mortality rates by census division and the percent of the adult male population with occupation in any type of farming (r = 0.24) or in dairy farming (r = 0.32). The results do not support the hypothesis that the apparently high risk of prostatic cancer in rural Manitoba is related to farming.

In a California review Ernster et al (1979) did a retrospective analysis based on death certificates in 2 California counties to look at the possible relationships between certain occupations and prostatic cancer. Early data came from large-scale studies that examined mortality by cause across occupational groups rather than focusing specifically on the occupational distribution of prostatic cancer patients. No consistent findings emerge from an examination of these reports. No previous study has attempted to compare prostatic cancer cases and suitably matched noncancer controls drawn from the general population in terms of possible differences across a broad range

of occupations. This was the objective of the present study. Cases included men who died of prostatic cancer in two northern California counties, Alameda and San Francisco, during the period 1968 to 1972. Using state death tapes, controls for each death were computer matched for sex, age within two years, race, date of death, and county of residence, excluding any other cancer or genitourinary deaths. Although the odds ratio and the difference between the numbers of observed and expected subjects within any given occupation/industry could be evaluated statistically, the presentation of significance levels of such testing could be misleading because a large number (>100) of comparisons were performed and the analysis was done with no a priori hypotheses. Various occupations/industries were investigated in an exploratory manner and, furthermore, the same data were used for investigating both occupation and industry. To replace the traditional level of significance of $p \leq .05$, they chose as the criterion for reporting results an odds ratio of 2.0 or greater derived from observations based on three or more matched sets. A total of 368 prostatic cancer deaths and 1,104 controls were included in the Alameda County study population and 334 deaths and 668 controls from San Francisco County. Their finding of an increased risk for men in the "horticultural services" industry is consistent with previous reports of an association with occupational "exposures to fertilizers" and farming. Likewise, the finding of an increased risk for "motor vehicle dealers" might parallel the sugestion elsewhere that cases of prostatic cancer report an excess of occupational "exposure to automobile exhaust fumes" compared with controls. They believe that this study tentatively supports the possibility that selected occupations and industries have an excess risk for the development of prostate cancer. Once again, differences found here cannot be accounted for by age and race, factors which were controlled in the analysis. It appears that it would be worthwhile to further investigate farming and other agricultural/horticultural workers; shipfitters; compositors and typesetters; and those who handle chemicals.

Arakai (1981) determined the characteristics of patients with benign prostatic hypertrophy (BPH) in a matched pair

analysis of 100 patients with BPH and 100 controls. Statistically significant epidemiological characteristics of patients with BPH included (1) not working in agricultural forestry or fishing, (2) not being exposed to environmental pollution at work, (3) having the first wet dream before age 20, (4) spending at least 10 minutes when having sexual intercourse one time, (5) no history of having impotence for greater than 1 month, and (6) no family history of breast cancer or personal history of gastric ulcers. Incidence of BPH was not related to family history of uterine cancer, prostatic cancer, ovarian cancer, or other cancer besides breast cancer.

## Bladder Cancer

Blair and Watts (1980) examined the occupational statements on a large number of death certificates from Wisconsin, a state with a large dairy industry. Between 1968 and 1976 there were 1,386 deaths from bladder cancer among white males 30 years or older. For each death certificate giving bladder cancer as the underlying cause, a control certificate, matched on race, sex, age and year of death, and county of residence was chosen from other causes of death. Occupation, as recorded on the death certificate, was coded according to the 1960 Census. Odds ratios (OR), as calculated by the McNemar test, significance tests, and 95% confidence limits were computed for each category according to matched pair procedures using a program developed by Rothman and Boice. The sample size in this study allowed detection of statistically significant ORs as low as 1.35 (much lower than the OR of 3.15 from the Roswell Park data). Farming was the most common occupation observed (20% of the cases and controls), but the risk of bladder cancer among farmers was not unusual (OR = 0.97). Likewise, the ORs did not differ significantly from unity when the matched pairs were stratified according to year of birth or death, age at death, or by the level of dairy production in the decedent's county of residence. Their results based on limited death certificate information fail to confirm the report of an excess risk of bladder cancer among dairy farmers.

Gottlieb and Pickle (1981) did a preliminary investigation to study reasons for reported excessive mortality from cancer of the urinary bladder in Louisiana. Death certificates of 347 who died of another cause in 19 Louisiana parishes during 1960-1975 were examined. Such factors as age at death, sex, race, year of death, and parish of residence were matched. Transport equipment workers and white mechanics also may be at increased risk for bladder cancer, along with young farmers of both black and white races.

Maegawa et al (1979) observed that there was a tendency toward an annual increase in bladder cancer from 1959-1976, as shown by 2,258 autopsy cases including 1,611 males, 636 females, and 11 cases in which the sex was not given. The age distribution was monophasic with a peak in the 60's. By occupation, the incidence was highest among the jobless, followed by housewives, office workers, and farmers, showing no specific occupation. Renal disease was the only complication. The lymphatic system was the most frequent metastatic site, followed by the lungs and then the liver.

Decoufle and Stanislawczyk (1973) analyzed lifetime occupational histories of patients admitted to Roswell Park Memorial Institute (RPMI), Buffalo, New York between 1956 and 1965 for specific forms of cancer and compared with those of patients diagnosed with non-neoplastic conditions. Relative risk estimates for different cancers within a variety of occupational groups were computed according to classic case-control methodology to indicate the degree of association between an occupation and cancer. The results were presented separately for men and women and referred to persons ever employed in an occupation as well as those employed for five or more years. Risk estimates for certain cancers were adjusted for differences in smoking habits between cancer cases and controls. Among the many comparisons shown in the report, selected possible high-risk occupations were pointed out as examples of findings which are consistent with prior observations and others that warrant

further follow-up. Among these were <u>bladder cancer</u> in leather workers and <u>dairy farmers</u>, lung cancer in brickmasons and smeltermen, and oral cancer in printing workers. Dairy farmers exhibit a very striking increase in bladder cancer, while other farmers show a deficit for this site - a finding which is not readily explainable.

## Renal Cancer

Milham (1976) analyzed the occupational and cause-of-death information on about 300,000 Washington State male (age 20+) death records for the years 1950-1971 using an age and year of death standardized proportionate mortality ratio approach. A detailed cause of death analysis (160 causes) was published for each of 194 occupational classes. The occupational mortality findings were compared with those of the Registrar General, for England and Wales and with the one 1950 U.S.study. Wheat and grain farmers and cattle ranchers showed an excess of kidney cancer with PMR = 151 and PMR = 211 respectively.

## <u>Central Nervous System Cancer</u>

Musicco et al (1982) compared patients with gliomas of the central nervous system hospitalized during the period January 1979-March 1980 at the Neurological Institute C. Besta of Milan with controls admitted to the Institute in the same period for non-neoplastic neurologic diseases or benign tumors. The comparison was based on occupational history, smoking habits, and alcohol consumption. Two analyses were carried out: the first by case-control pairs matched for age, sex, and residence; the second by age, sex, and residence stratification. Patients with glioma were more likely than controls to have worked in agricultural activities and showed a relative risk of 5.0 (P = 0.043) in the matched analysis and 1.9 (P = 0.113) in the analysis by stratification. This high risk was confined to those who performed agricultural work after 1960, suggesting a possible

etiologic role of exposure to organic pesticides, fertilizers, and herbicides, which have only recently been commonly used in Italy. No significant difference was observed between cases and controls in regard to other analyzed occupations and habits.

Gold et al (1979) conducted an exploratory case-control study in 15 hospitals in the Baltimore, MD, SMSA of possible etiologic factors associated with brain tumors in children. Eighty-four children with brain tumors were compared to normal children and to children with other malignancies. Parents of these children were interviewed about a variety of possible etiologic factors. No significant differences were observed between children with brain tumors and children in either of the two control groups with regard to occupational chemical exposures of their parents either prenatally or postnatally before diagnosis. To determine whether children had been exposed to insecticides, parents were asked about exterminations in the household prior to diagnosis of the index child. The results showed that more children with brain tumors than normal controls were reported to have had such exposures, with the odds ratio of 23. approaching statistical significance (p = .10). Children with brain tumors did not differ from children with other cancers with regard to such exposures. It is possible that insecticides may contain nonspecific chemical carcinogens which may induce not only brain tumors in children but cancers in general.

Milham (1976) analyzed the occupational and cause-of-death information on about 300,000 Washington State male (age 20+) death records for the years 1950-1971 using an age and year of death standardized proportionate mortality ratio approach. A detailed cause of death analysis (160 causes) was published for each of 194 occupational classes. The occupational mortality findings were compared with those of the Registrar General, for England and Wales and with the one 1950 U.S. study. Cattle and dairy farmers showed an excess of brain tumours with PMR = 176 and PMR = 187 respectively.

Choi et al (1970) compiled data on the pattern of occurrence in the general population in Minnesota and possibly the roles of

host and environmental factors, of all patients with primary central nervous system neoplasms who died in the five-year period 1958-1962. A total of 760 cases were found. The epidemiologic variables were compared with the distribution of these variables in the general population. Bimodality of age-sex specific mortality rates, differential sex selectivity by types of the tumors, and significantly higher mortality among farm residents and foreign-born persons (especially younger age groups) were among the significant findings. These findings may imply multiple causalities or factors differing by tumor type, age, sex, etc. No geographic gradient of the rates (by county) or differential rates by occupation were noted. The high mortality of farm residents correlates with the theory that a possible relationship exists between toxoplasmosis and certain brain tumors. The higher mortality among the foreign-born population may imply that the origin of brain tumors among younger age groups resides in congenital factors, either innate or via the fetal environment, or via the environment in early childhood, both peculiar to the place of birth. In view of the fact that several countries of birth, including Norway, Germany, Canada and Finland, were among those foreign countries from which immigrants had excess proportions of brain tumor deaths, more extensive observations on the foreign-born population from such countries and in such countries may be worthwhile.

Schuman et al (1967) investigated the relationship of central nervous system neoplasms to toxoplasma gondii infection. To test this hypothesis, the retrospective study design involved the utilization of hospitalized brain tumor cases and a series of hospitalized matched controls, each tested for toxoplasma antibody by the Saabin-Feldman dye-test technique as evidence of infection. The study began in June, 1963. All cases of histologically proven primary central nervous system tumors diagnosed in the four designated hospitals between January 1 and June 20 of that year were located by a search of hospital records for all patients admitted during this period. In addition to this retrospective group, another group of brain and spinal cord tumor patients newly admitted from June 21, 1963 until June 30,

1964 coming from all parts of the state and diagnosed by clinical suspicion, but not necessarily proved histologically at the time of their admission, were included in the study group.

For purposes of this study, infection with Toxoplasma gondii was deemed to have occurred if the Sabin-Feldman dye-test was positive in subject serum dilutions of 1:1 or greater. A total of 171 cases of primary central nervous system neoplasms was collected in the 18-month period from the four designated hospitals. The toxoplasma dye-test results among verified cases and matched controls indicates that the excess in proportion of total dye-test positives among the CNS neoplasm cases is statistically significant ($p = 0.021$). The data presented herein do, indeed, support the hypothesis that toxoplasma infection and human gliomas are related.

## Skin Cancer

Wiklund (1983) a Cancer-Environment Registry was established in Sweden in 1978. A study of the register revealed that for persons engaged in agricultural work, the risk for most types of cancer was lower than the respective national averages. For cancer of the trachea, bronchus, lung and pleura, the ratio of observed to expected numbers of cases is 0.39 (observed 934, expected 2375). The difference is statistically significant. For laryngeal cancer the ratio is 0.38 (observed 94, expected 248), which likewise is significant. Primary cancer of the liver and tongue also show less than expected frequency. The risk of cancer of the lip, however, is greater by a factor of almost 2 than the national average, which is consistent with results from other studies.

Michailov et al (1981) studied the association of various dermatologic diseases with occupational exposure to UV irradiation. Occupations were recorded for 6,836 patients with solar keratosis, 3,816 patients with skin cancer, 160 patients with dermatitis associated with exposure to bituminous coal products dissolved in petroleum (or mineral oil), 20 patients with toxic melanodermia, 6 patients with photoallergic

dermatitis, and 45 patients with solar urticaria. Among the skin cancer patients, there were 2,128 men and 1,688 women. Thirty-six percent of these patients were farmers and 6% were farm workers; therefore, it was concluded that 42% of the skin cancers were associated with occupational exposure to UV irradiation from the sun. Eighty-four percent of the skin cancers were located on the face, 11% were on the lower lip, and 1% were on the back of the hand; therefore, the overwhelming majority of skin cancers occurred on skin surfaces that were normally not covered and received the greatest exposure to the sun.

Lindquist et al (1981) determined the standardized morbidity ratios (SMR) of lip and non-melanomatous skin cancer (basal-cell carcinoma excluded) of the head and neck in males for different occupational groups in Finland. The data on all cases of these types of cancer diagnosed in Finland in the age group 35-69 years in 1971-75 were supplemented by information on occupations from the 1970 census (Central Statistical Office of Finland). The expected numbers of cases were based on the age and occupation-specific numbers of person-years computed by the Central Statistical Office, and the age-specific incidence rates of lip and skin cancers among the economically active population. The highest SMR of lip cancer among all the occupational groups was found in agriculture, forestry and fishing (1.64). In contrast, the SMR of skin cancer was not higher than expected in occupations related to agriculture and forestry. Significantly lower than expected risks of lip cancer were observed among highly educated white-collar workers, among whom the risk of contracting skin cancer was the highest (technical, scientific, humanistic and artistic work). The morbidity of both lip and skin cancers varies considerably by occupation, and the risks seem to be, at least in part, inversely related. Thus, it is probable that there are also differences in the risk factors, contrary to several earlier suggestions.

In a British study Whitaker et al (1979) observed that during the three years 1967-69, 781 cases of squamous cell carcinoma of the skin were reported to the Manchester Regional

Cancer Registry. The proportions of males to females were significantly different (P < 0.001) among the skin cancer sites. The age-specific incidence rates were significantly different (P < 0.001) between the sexes for the five-year age groups of 55 years and above. Full occupational histories were obtained on 598 (77%) patients; a further 148 (19%) patients gave one main occupation only, while the remaining 35 (4%) patients were untraced. The numbers of patients observed in broad occupational groups (occupational orders) were compared with the numbers expected using the 1931 and 1951 censuses. For all skin cancer sites combined the occupations of farming and textiles were found to have highly significant excesses of 150% and 135% respectively for males. The corresponding excesses for females were 30% for textile workers and varied from 1140% to 590% for farmers, but only for the farmers were the excesses highly significant. For both male and female patients no significant associations were found between the skin site and either eye colour, residence in the tropics or smoking habit.

Scher et al (1981) observed that in West Virginia from 1959 to 1975 there were 279 deaths caused by malignant melanoma. From 1959 to 1967 there were 8.4 such deaths per year and from 1968 to 1975, 25.4 per year (2P < .0005). This trend was observed throughout the state. The population-adjusted melanoma mortality of 1.45 per 100,000 from 1968 to 1975 contrasts with a rate of only 0.48 per 100,000 during the earlier period from 1959 to 1967. The rate of increase was greater in the southern portion of the state. The highest melanoma mortality was seen in the state's major agricultural area, while the lowest rate was seen in its most densely populated urban region. In our community, 102 new melanoma cases were diagnosed from 1969 to 1978. From 1969 to 1973, there were 33 new cases, 6.6 per year, and from 1974 to 1978, 13.8 per year (p < .01). Men tended to be older at the time of diagnosis. The most common locations of the primary tumors were the lower extremity in women and the trunk and head and neck in men.

Paletta (1980) observed that squamous cell carcinoma of the skin is the second most common malignant tumor of the skin. The

frequency of occurrence in no way approaches the number of cases of basal cell carcinoma seen in a surgical practice, that exposure to sun was an inciting factor. Skin cancer in farmers, sailors, redheads, and individuals with a reddish complexion frequently occurs because of exposure to the sun.

Zagula-Mally et al (1974) surveyed the frequency of skin cancer and solar keratoses in a rural Tennessee county using techniques of cluster sampling. Trained nurses and dermatologists interviewed and examined 978 Caucasian adults. Of these, 16.3% were found to have solar keratoses (usually multiple), and 4.4% appeared to have skin cancers.

Friedrich (1972) reports a case of carcinoma in situ of the vulva in identical twins related to chronic contact of the vulvar skin with arsenical insecticides during farming operations. This report emphasizes the role of hereditary predisposition in the development of cancer and serves to refocus attention on arsenic, a common constituent of insecticides and detergents, as an etiologic agent in carcinomas of the skin.

## Assessment of Causation

The following tables summarize the evidence that associates farm work with cancer. Each table relates a specific group of site specific cancers to farm work and assesses the quality of evidence utilizing the diagnostic tests for causation.

ASSESSMENT OF CAUSATION: FARMING AND HAEMATOLOGICAL MALIGNANCY

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Gallagher et al (1984) (PMR = 122) for leukemia in male farmers in British Columbia aged 20 years or more (proportional mortality study)<br><br>Cantor and Blair (1984) showed farmers at an elevated risk -(odds ratio =1.4) of death due to multiple myeloma >65 years old (OR=1.5) <65 years old (OR = 1.1). High chicken inventory (OR=1.6) High fertilizer use (OR = 1.7) High # of acres treated with pesticides (OR = 1.9) (case-control study)<br><br>Buesching and Wollstadt (1984) indicate significantly elevated risk among farmers for non-Hodgkin's lymphoma (SMR = 2.65)(cross-sectional study)<br><br>Burmeister et al (1983) (OR = 1.48) for multiple myeloma in farmers (OR - 1.26) for non-Hodgkin's lymphoma in farmers. Greater in those born after 1890 and on hog or chicken farms and farms using increased herbicides and insecticides (case-control study)<br><br>Gallagher et al (1983) History of agricultural work associated with an elevated risk of multiple myeloma (Rel. risk 2.2, p = 0.01)(case control study)<br><br>Cantor (1982) Frequency of farming occupation among cases of non-Hodgkin's lymphoma (OR = 1.22), greater among farmers < 65 years old (OR = 1.7), < 65 years old and risk of reticulum cell carcinoma (OR = 2.7), for younger farmers on general farms (OR = 3.2)<br><br>cont'd | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Cantor (1982) cont'd for younger farmers of small grain acreage and acres treated with insecticides (OR = 6.6) -for younger farmers on wheat farms (OR = 4.4)(case-control study) | |
| | Burmeister et al (1982) Leukemia mortality among farmers (OR = 1.24, p <0.05) Higher if born after 1890 (OR = 1.36) Dying after 1970 (OR = 1.36) and dying at age 65 or younger (OR = 1.36) Chronic lymphocytic leukemia elevated in areas of high soybean production (OR = 2.2) and high # of acres treated with herbicides (OR = 1.89). Unspecified leukemia elevated in areas of high corn production (OR = 4.63), high numbers of milk cows (OR = 4.94), high # of egg-laying chickens (OR = 2.47) (case-control study) | |
| | Blair and White (1981) Risk of leukemia among dairy farmers born after 1897 (OR = 1.5) or dying before age 71 years (OR = 1.35) for dairy farmers (OR = 1.4), for farmers in counties with heavy use of fertilizers (OR = 1.42)(case-control study) | Blair and White (1981) Risk of leukemia among farmers and dairy farmers was slight (OR = 1.10) and statistically nonsignificant. (case-control study) |
| | Hardell et al (1981) Exposure to phenoxy acids and chlorophenols may be causative factor in Hodgkin's and non-Hodgkin's lymphoma (Rel. risk = 6.10) (case-control study) | |
| | Burmeister (1981)(PMR = 1.1) for leukemia (PMR = 1.27) for multiple myeloma in farmers (proportional mortality study) | |
| | Donham et al (1980) Males <20 years old have a higher risk of acute lymphoid leukemia (ALL) in rural communities (Standard incidence ratio = 132) Males >60 years higher risk of all chronic lymphocytic leukemia (Standard incidence ratio = 109) | |
| | cont'd | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Donham cont'd | |
| | Association between numbers of cows and human leukemia incidence (O/E = 1.4), for dairy cattle (O/E = 1.47) also an increase in human ALL in residents in counties where BLS has been diagnosed (O/E = 1.22)(proportional mortality study) | |
| | | Linos (1980) Farming occupations did not show a significantly different relative risk for leukemia (Rel. Risk = 0.7) (case-control study) |
| | Blair and Thomas (1979) an elevated risk of leukemia among farmers (Odds ratio = 1.25) if born after 1900 and dying before age 66 (OR = 1.83) Elevated risk for farmers in heavy corn-producing counties (OR = 1.44) (case-control study) | |
| | Linos et al (1978) A significant number of leukemia patients were farmers in an incidence study of leukemia in Olmstead County (8 observed, 2.8 expected) ( cross-sectional study) | |
| | Milham (1971) A statistically significant association between farming occupations and death from leukemia and multiple myeloma ($p < 0.05$) Strongest in men <60 years old. Poultry farmers had highest case excess (case-control study) | |
| | Fasal et al (1968) elevated mortality from leukemia for male and female farm residents (SMR = 114) (proportional mortality study) | |
| | Priester et al (1970) showed a 95% probability of detecting 2.4 fold or greater increase in human cancer mortality associated with bovine leukosis (prospective study) | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| CONSISTENCY | Gallagher et al (1981), Burmeister et al (1982), Blair and White (1981), Blair and Thomas (1979), Milham (1971, Fasal (1968), Cantor and Blair (1984), Gallagher et al (1983), Cantor (1982), Hardell (1981), had similar odds ratio in retrospective studies. | Blair and White (1981) showed odds ratio not statistically significant for leukemia (cross-sectional study)<br><br>Linos (1980) showed similar results to Blair and White (1981) not significantly different relative risk. (case-control study) |
| SPECIFICITY | No prospective studies done | |
| TEMPORAL RELATIONS | Hardell (1981) linked prior exposure to phenoxy acids and chlorophenols to increased risk (case-control study) Another factor noted in all studies is the higher risk associated with farmers $\leq$ 65 years old. This could be a reflection of the introduction of pesticides in the 1900-1920's and increased usage in the 1940's. | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| BIOLOGICAL PLAUSIBILITY | Bovine Leukosis virus can induce antibody production in other species (Piper et al 1975) | |
| | The B-cell origin of most leukemias, non-Hodgkin's lymphoma, and multiple myeloma suggests that these diseases could potentially share etiologic determinants (Blattner 1980) | |
| | Previous investigations of leukemia or NHL have suggested zoonotic oncornoviruses (Heath 1975) | |
| | Benzene a constituent of some pesticides has been linked with both CLL and MM (Tarceff 1963) | |
| | Increased production of tumours in mice exposed to phenoxy acids (Hansen 1970) | |
| | Recent studies of 2,4,6-trichlorophenol in rats showed an increased incidence of malignant lymphomas and leukemias (NCI 1979) | |

ASSESSMENT OF CAUSATION: NASAL CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Hardell et al (1982) A seven fold increase of nasal and nasopharyngeal cancer after exposure to chlorophenols present in wooddust (case-control) | Hernberg et al (1983) No association found for agricultural chemicals and nasal cancer (case-control study) |
| CONSISTENCY | | Findings not consistent. No prospective studies done. |
| SPECIFICITY | Studies looked at chemicals used in agriculture. Hernberg (1983) and Hardell et al (1984) | |
| TEMPORAL RELATIONSHIP | No prospective studies done | |
| DOSE-RESPONSE RELATIONSHIP | No prospective studies done | |
| BIOLOGIC PLAUSIBILITY | Animal studies on 2,4,5-T and 2,4,5-T-phenoxyethanol showed them to be carcinogenic Muranyi-Kovacs (1976) | |

ASSESSMENT OF CAUSATION: LARYNGEAL CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Flanders et al (1984) Risk ratios were above 3.0 for farmers with regards to laryngeal cancer. All farmers (Rel. Risk = 4.9) Grain farmers (Rel. Risk = 6.9)(case-control study) | |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | No prospective studies done | |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| IOLOGICAL PLAUSIBILITY | | |

ASSESSMENT OF CAUSATION: LUNG CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Blair et al (1983) Elevated (SMR = 135) for lung cancer in pesticide applicators SMR rose with number of years licenced.<br><10 years (SMR = 101)<br>10-19 years (SMR = 155)<br>≥20 years (SMR = 289) or if licenced after age 40 (SMR = 115) and before age 40 (SMR = 234)<br>(proportional mortality study)<br><br>Rothschild and Mulvey (1982) Rel. Risk = 2.4 of lung cancer for sugar cane farm workers. (cross-sectional study)<br><br>Barthel (1981) significantly increased SMR = 2.0 for lung cancer in pesticide exposed male agricultural workers<br>(proportional mortality study) | |
| CONSISTENCY | Retrospective studies in agreement Blair et al (1983) Barthel (1981)<br><br>No prospective studies done | |
| SPECIFICITY | Blair et al (1983) Pesticides, particularly organophosphorus and organochlorines are cited as the putative agents<br><br>Barthel (1981) lists pesticides used at that time in the GDR as the possible putative agent. | |
| TEMPORAL RELATIONSHIP | Exposure to pesticides occurred before onset of carcinoma<br>Blair et al (1983), Barthel (1981) | |
| DOSE-RESPONSE RELATIONSHIP | Blair et al (1983) showed change in risk with length of exposure according to age of being licenced and number of years licenced. | |
| BIOLOGICAL PLAUSIBILITY | A considerable number of pesticides have been shown to be carcinogenic in animals. Durham and Williams (1972), Falk et al (1965) | |

ASSESSMENT OF CAUSATION: FARMING AND SOFT TISSUE SARCOMA

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Balarajan and Acheson (1984) farmers, farm managers and market gardeners had a Rel. Risk = 1.7) for developing soft-tissue sarcoma (STS) ( case-control study) | |
| | Eriksson et al (1981) (Re. Risk = 6.4) for developing STS after exposure to phenoxy acids (case-control study) | |
| | | Zack and Suskind (1980) No apparent excess in deaths from malignant neoplasms after exposure to 2,4,5-T after a process accident (cohort study) |
| | | Cook et al (1980) No statistically significant increase of malignancy. Exposure to 2,3,7,8-tetrachlorodebenzo-p-dioxin in a manufacturing plant (cohort study) |
| | | Ott et al (1980) No adverse effects observed after exposure to 2,4,5-T and 2,4,5-Trichlorophenol in a manufacturing plant (cohort study) |
| | Hardell and Sandstrom (1979) (Risk Ratio = 5.7) for STS after exposure to phenoxy acids and chlorophenols (case-control study) | |
| CONSISTENCY | | No consistency between prospective studies Zack and Suskind (1980), Cook et al (1980), and Ott et al (1980) and retrospective studies done by Eriksson et al (1981) and Hardell and Sandstrom (1979) |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| SPECIFICITY | Balarajan and Acheson (1984) Eriksson et al (1981) and Hardell and Sandstrom (1979) identified phenoxy acids and chlorophenols as the putative agent | |
| | | Ott et al (1980), Cook et al (1980) and Zack and Suskind (1980) Chlorophenols and phenoxyacetic acids were the putative agents. |
| TEMPORAL RELATIONSHIP | Erikson et al (1981) prior exposure of 36.5% of the cases to phenoxy acids. Hardell and Sandstrom (1979) prior exposure of 22.7% of cases to phenoxy acids. | |
| | Eriksson et al (1981) took latency into account by excluding cases exposed within 5 years before diagnosis of diseases. | |
| | | Ott et al (1980) measured air levels of TCP, 2,4,5-T and 2-4-D for specific jobs done in 1969 and used time spent in these jobs to determine exposure. Also looked at latency period. |
| | | Zack and Suskind (1980) followed workers for 30 years after an accident at high exposure to TCDD |
| | | Cook et al (1980) followed workers from 1964-1978 who had developed chloracne from 2,3,7,8-tetrachlordibenzo-p-dioxin exposure |
| DOSE RESPONSE | | Ott et al (1980) exposure expressed in terms of length of employment. No dose-response found. |
| | | Cook et al (1980) cohort divided into low and high exposure groups: No dose-response found. |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| BIOLOGICAL PLAUSIBILITY | Animal studies on 2,4,5-T and 2,4,5-T - phenoxyethanol showed them to be carcinogenic (Muranyi-Kovacs 1976)<br><br>Inhibition of testicular DNA synthesis showed decreased thymidine uptake for 4 phenoxy acids (Seiler 1979)<br><br>2,7,-dichloro-dioxin isomer probably carcinogenic in male mice and caused marginal increased incidence of leukemias and lymphomas (NCI 1979)<br><br>Results of mutagenic properties for chlorinated dioxin isomers varied from weakly positive to positive (Ashby 1982) | |

ASSESSMENT OF CAUSATION: OESOPHAGEAL CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | | Faivre et al (1981) Lower risk amongst agricultural workers (Rel. Risk = 0.38, $p < 0.05$)(Descriptive Study)<br><br>Decoufle and Stanislawczyk(1973 no increased risk in farmers and managers (Rel. Risk = 0.997 (case-control study) |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | No prospective studies done | |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| BIOLOGICAL PLAUSIBILITY | | |

ASSESSMENT OF CAUSATION: STOMACH CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Buesching and Wollstadt (1984) Iowa farmers increased risk (PMR= 1.14) for stomach cancer (proportional mortality study) | |
| | Burmeister et al (1983) Farmers showed an increased risk (O R.=1.32) for stomach cancer (case-control study) | |
| | Burmeister (1981) Mortality rates significantly higher for farmers for stomach cancer (PMR=1.14) (proportional mortality study) | |
| | Armijo et al (1981) Number of years working in agriculture showed a significant risk for stomach cancer (p <0.05)(case-control study) | |
| | Amadori et al (1980) Higher risk for gastric cancer in rural area. Statistically significant difference between rural and urban area (p <0.0001)(cross-sectional study) | |
| | Zaldivar and Witterstrand (1975) Positive correlation between exposure to nitrate fertilizers and gastric cancer death rates (p <0.00005) (correlation study) | |
| | Armijo and Coulson (1975) Correlation found between death rates from stomach cancer and cumulative per capita exposure to nitrogen fertilizers. Three agricultural provinces show a median rate of 50.1 per 100,000 mortality rate for stomach cancer in comparison to other areas with 21.6/100,000 (correlation study) | |
| | Zaldivar and Robinson (1973) A statistically significant association between exposure to sodium nitrate fertilizer and stomach cancer p <0.02. Male farmers accounted for 31.2% of all male deaths from stomach cancer. (correlation study) | |
| | Milham (1971) Increased mortality rate for stomach cancer for farmers (PMR=117), for dairy farmers (PMR=143)(proportianal mortality study) | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| CONSISTENCY | Similar risk ratios in retro-spective studies.<br>Buesching and Wollstadt (1984)<br>Burmeister et al (1983)<br>Burmeister et al (1981)<br>Armijo et al (1981)<br>Zaldivar and Mitterand (1975)<br>Armijo and Coulson (1975)<br>Zaldivar (1973)<br>Milham (1971) | |
| SPECIFICITY | Several studies implicate nitrogen fertilizers as the putative agent.<br>Armijo et al (1981)<br>Amadori et al (1980)<br>Zaldivar and Wittersand (1975)<br>Armijo and Coulson (1975)<br>Zaldivar and Robinson (1973) | |
| TEMPORAL RELATIONSHIP | Exposure to nitrogen fertilizers occurred before onset of carcinoma<br>Amadori et al (1980)<br>Zaldivar and Wittersand (1975)<br>Armijo and Coulson (1975)<br>Zaldivar and Robinson (1973) | |
| OSE-RESPONSE RELATIONSHIP | | |
| BIOLOGIC PLAUSIBILITY | N-nitroso compounds induce tumours in animals<br>Magee and Barnes (1967) | |

## ASSESSMENT OF CAUSATION: LIVER CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Stemhagen et al (1983) (odds ratio = 1.89) for male farm labourers developing primary liver cancer (retrospective case-control) | |
| | | Falk et al (1981) Risk not higher among farmers for hepatic angiosarcoma (case-control) |
| | Milham (1974) Farmers have an elevated PMR for liver cancer (PMR=>150) (proportional mortality study) | |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | Stemhagen et al (1983) Exposure of interest was arsenical pesticides | |
| | | Falk et al (1981) identified inorganic arsenic as one of the causative factors in HAS |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| BIOLOGICAL PLAUSIBILITY | | No indication of carcinogenesis was found in 2-year studies of 600 rats and 48 dogs Byron et al (1967) |
| | | IARC noted arsenic negative for carcinogenesis and the few positive tests were defective and should be repeated (WHO 1973) |

ASSESSMENT OF CAUSATION: PANCREATIC CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Gold and Diener (1981) increased risk of pancreatic cancer found for living on a farm and having farm animals (case-control study) | |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | No prospective studies done | |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| BIOLOGICAL PLAUSIBILITY | | |

ASSESSMENT FOR CAUSATION: COLORECTAL CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Abu-Zeid et al (1981) significantly increased risk to cancer of the colon and rectum associated with living on a farm (case-control study)<br><br>Pratt et al (1977) association between colorectal cancer in adolescents and exposure to farm or agricultural chemicals (descriptive survey) | |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | No prospective studies done | |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| BIOLOGICAL PLAUSIBILITY | | |

ASSESSMENT OF CAUSATION: CANCER OF THE MALE REPRODUCTIVE SYSTEM AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Mills et al (1984) Significant association between testicular cancer and agriculture (OR=6.27, $p < 0.05$) and between testicular cancer and work in the crude petroleum oil and natural gas industry (OR=2.29)(case-control study) | |
| | | Brown and Pottern (1984) No increase in testicular cancer risk for either ever or current farming (OR=0.9 and OR=0.6) For rural residence (OR=0.8) (case-control study) |
| | Brown and Pottern (1984) Data analyzed for current farmers who grew up in the south (OR=1.4) for testicular cancer (case-control study) | |
| | | Jensen et al (1984) No indication of an increased risk associated with farming and related activities (OR=1.00)(case-control study) |
| | McDowell and Balarajan (1984) Excess risk of testicular cancer in farmers (OR=1.89)(case-control study) | |
| | | Van Shepen et al (1983) No association between high risk of prostatic cancer in rural Manitoba and farming (OR=1.28) but not statistically significant (case-control study) |
| | Ernster et al (1979) Increased risk for men in the "horticultural Services" industry for prostatic cancer (OR=2.8) also increased risk for "motor vehicle dealers" or exposure to automobile exhaust fumes (OR=4.5) (case-control study) | |
| | Tallerman et al (1974) A significantly higher incidence ($p < 0.0001$) of all testicular neoplasms in a rural district (descriptive study) | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | Mills et al (1984) cites infection or zoonotic viruses as the putative agent in farming. Millo et al (1984) and Ernster et al (1984) cite gasoline or exhaust fumes as the possible agent. | |
| TEMPORAL RELATIONSHIP | No prospective studies done | |
| DOSE-RESPONSE | No prospective studies done | |
| BIOLOGICAL PLAUSIBILITY | Mutagenic activity detected in the exhaust from gasoline engines Ohnishi et al (1980) | |

ASSESSMENT OF CAUSATION OF FEMALE REPRODUCTIVE SYSTEM AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Donna et al (1984) Positive association has been found between herbicide exposure and ovarian mesotheliomas (OR = 4.38)(case-control study) | |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | Donna et al (1984) - definite exposure to herbicides and brand name and probable exposure - the subjects were farmers (after 1960 usage of herbicides began in Italy) or they resided in areas where there was a known herbicide usage. No exposure to asbestos. | |
| TEMPORAL RELATIONSHIP | No prospective studies done | |
| DOSE-RESPONSE RELATIONSHIP | No prospective studies done | |
| BIOLOGICAL PLAUSIBILITY | Recent animal studies showing herbicides used in the area were carcinogenic for animals. Donna et al (1979-80) Donna et al (1981) | |

ASSESSMENT OF CAUSATION: BLADDER OR KIDNEY CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Decoufle and Stanislawczyk (1973) increased risk of bladder cancer in farmers (Rel. Risk 3.15) (case-control study)<br><br>Milham (1974) showed increased risk of cancer of the kidney in wheat farmers PMR = 151 and cattle ranchers PMR = 211 (proportional mortality study) | Blair and Watts (1980) No excess risk of bladder cancer among dairy farmers (OR = 0.97)(case-control study) |
| CONSISTENCY | No prospective studies done | |
| SPECIFICITY | | |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| BIOLOGICAL PLAUSIBILITY | | |

## ASSESSMENT OF CAUSATION: GLIOMAS AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Musicco et al (1982) Patients with glioma were more likely to have worked in agriculture (Rel. Risk = 5.7, p = 0.043) especially if worked after 1960 (case-control study)<br>Gold et al (1979) More children with brain tumours were found to have had exposure to insecticides more than normal children (Odds ratio = 2.3, p = .10)(case-control study) | |
| | Choi et al (1970) Excess number of rural farm residents among cases that developed brain tumours (p <0.05)( correlation study) | |
| | | Choi et al (1970) Slight excess of farm workers amongst the brain tumour cases but this was not statistically significant (cross-sectional study) |
| | Milham (1974) (PMR = 176) for cattle ranchers and (PMR = 187) for dairy farmers for brain cancer (proportional mortality study) | |
| | Schuman et al (1967) Toxoplasma infection and gliomas in humans are related (p = 0.021) | |
| CONSISTENCY | Evidence in all retrospective studies similar for farm residents. Musicco et al (1982), Choi et al (1970), Schuman et al (1967) and Milham (1971). No prospective study done. | |

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| SPECIFICITY | Choi et al (1970)<br>Schuman et al (1967) implicated Toxoplasma gondii as a possible putative agent. | |
| TEMPORAL RELATIONSHIP | Mussico et al (1982) Since high risk (Rel. risk = 5.7) after 1960 and lower risk (Rel. Risk = 2.5) before 1960 and since pesticides were first introduced in Italy in 1960 this could indicate a prior exposure to pesticides before diagnosis of disease (case-control study)<br>Schuman et al (1967) performed Sabin-Feldman test to determine if exposure to Toxoplasma gondii had occurred. The excess in proportion of total dye-test positives among the CNS neoplasm cases was statistically significant ($p = 0.021$) | |
| DOSE-RESPONSE RELATIONSHIP | Musicco et al (1982) Risk increases from 0.9 for thos who worked only before 1960 to 2.5 for those who worked before and after 1960 to 5.7 for those who worked only after 1960. The risk was higher for those who worked 10 or more years after 1960 (Rel. Risk = 4.8) than for those who worked less than 10 years (Rel. Risk = 1.9) suggesting a dose response relationship. This is consistent with the pattern of pesticide usage in Italy. | |
| BIOLOGICAL PLAUSIBILITY | Observation of "so-called gliomas" in chickens spontaneously and experimentally infected with Toxoplasma, Erichsen and Harboe (1953) | |

ASSESSMENT OF CAUSATION: SKIN CANCER AND FARMING

| | EVIDENCE FOR | EVIDENCE AGAINST |
|---|---|---|
| STRENGTH | Lindqvist et al (1981) (SMR = 1.64) for workers in agriculture for cancer of the lip (proportional mortality study) | |
| | Wiklund (1981) Incidence rate twice as high as expected for lip cancer (Proportional mortality study) | Lindqvist et al (1981) SMR = 1.07 for skin cancer in agriculture worker (cross-sectional study) |
| | Michailov et al (1981) 42% of skin cancers associated with UV irradiation from the sun (descriptive survey) | |
| | Whitaker et al (1979) Farmers show an excess of about 150% observed over expected for skin cancer. (mortality study) | |
| CONSISTENCY | Findings of Lindqvist et al (1981) and Whitaker et al (1979) not consistent regarding skin cancer | |
| SPECIFICITY | Probable cause of skin or lip cancer by solar radiation suggested by Lindqvist et al (1981) Whitaker et al (1979) and Michailov et al (1981) | |
| TEMPORAL RELATIONSHIP | | |
| DOSE-RESPONSE RELATIONSHIP | | |
| BIOLOGICAL PLAUSIBILITY | | |

CHAPTER FIVE

# REPRODUCTIVE HAZARDS AND FARM WORK

## Introduction

Personal tragedies are involved when defects are present at birth or appear in later life and the need for the detection of embryo/fetal toxic agents, the assessment of health risks, and the prevention of unfavourable outcomes of pregnancy, is evident. Though hundreds of chemicals, which have been listed by Shepard (1983), have induced embryotoxic effects in laboratory animals, very few have been shown to be teratogenic in human beings. However, an improved centralized system of registering birth defects, and the input of occupation onto hospital admission forms, would assist in the monitoring and prevention of congenital malformations induced by parental occupational exposure. Differences between animals and man in metabolism, inherent sensitivity, and levels of exposure may be responsible for this apparent discrepancy. Among the problems involved in conducting epidemiological studies is the detection of chemically-induced anomalies against a background of sporadic defects. The size of an epidemiological study necessary to detect changes in the rates of some abnormalities is so great that such studies are seldom conducted. Smaller studies result in inaccurate risk estimates.

Huang-Xing-Shu (1983) presented a lecture on preventing chemical damage to germ cells. From 1981 to 1982 in a county hospital in Zhejiang Province, 543 cases of males poisoned by pesticides were studied. Their ages were 18-45 and they were healthy prior to poisoning. The semen and testes of the patients were examined and they were questioned about sexual behavior and pregnant condition of their wives in order to know the extent of damage to the sperm and sexual behavior. The time intervals between occurrence of poisoning and semen examination were from 18-23 months. Among the 53 cases, 32 (60%) showed a decrease in sperm viability, 22 (41%) showed aspermia or decrease in number

of sperms, and 10 (19%) showed an increase of abnormal sperm. In addition, among 27 severe cases, shrinkage of testes was observed in 6 cases. The damage to testes tissue and sperm genesis in these patients persisted 1-2 years, as in workers exposed to DBCP. In a pesticide factory in Shandong Province after exposure to DBCP stopped, for two and a half years the sperm counts in 5 workers were still markedly decreased and accompanied by an increase of abnormal sperm. It is worth pointing out that shrinkage of testes in 5 of 6 cases occurred 3 months after poisoning. Whether the genesis of sperm could recover after the shrinkage of testes remains to be discovered. Among 27 women, 5 became pregnant, 1 delivered a normal child. Abortion occurred once in a woman whose husband had been damaged by DDVP and in another woman whose husband had been damaged by malathion.

## Male Reproduction

Brix (1982) reviewed environmental and occupational hazards to the fetus. Recently it has been recognized that men are not immune to reproductive hazards, either. Exposure to dibromochloropropane (DBCP), a pesticide used to kill worms, has been shown to lead to impaired spermatogenesis and azoospermia in men who manufacture it or spray it on crops.

Whorton et al (1977) discovered a number of cases of infertility among men working in a California pesticide factory. The suspected cause was exposure to the chemical 1,2-dibromo-3-chloropropane (DBCP). The major effects, seen in 14 of 25 non-vasectomised men, were azoospermia or oligospermia and raised serum-levels of follicle-stimulating hormone and luteinising hormone. No other major abnormalities were detected, and testosterone levels were normal. Although a quantitative estimation of exposure could not be obtained, the observed effects appeared to be related to duration of exposure to DBCP.

Whorton et al (1979) extended the preliminary communication. The company employing the affected men manufactures fertilizers and ammonia, and formulates pesticides for agricultural and

household use. In the various formulation processes, some 100 chemicals are used to produce approximately 200 different products, including organophosphorus compounds, halogenated hydrocarbons, and carbamates. Since 1962 the company had regularly formulated DBCP in a special agricultural chemical division (ACD). For several years before the problem of testicular function alteration was brought to their attention, men working in the ACD had become increasingly aware that few of them had recently fathered children. After an evaluation of five men revealed oligospermia or azoospermia in each, a total of 36 employees from ACD were studied in more detail. The most important findings were the following: The relationship between duration of chemical exposure and sperm count was striking. All 11 men with indisputably low sperm counts ($\leq$ 1 million) had been exposed for at least three years; none with sperm counts above 40 million had been exposed for more than three months. The mean level of follicle stimulating hormone (FSH) was significantly higher in the group of men exposed for at least three years each. No other important information on the health of the study subjects was brought to light by thorough medical examination accompanied by extensive laboratory evaluations.

There was a clear-cut difference in both the distribution of sperm counts and the median counts between the exposed men and the not-exposed men. Of the exposed, 13.1% were azoospermic, 16.8% were severely oligospermic, and 15.8% were mildly oligospermic. Among the controls, 2.9% were azoospermic, none were severely oligospermic, and 5.7% were mildly oligospermic. Under workplace conditions, DBCP appears to have a selective effect on the seminiferous tubules.

Levine et al (1983) observed that sperm count distributions among exposed and control groups at a dibromochloropropane (DBCP) manufacturing plant were remarkably similar. Yet reproductive histories from 60 exposed men obtained in conjunction with the semen analyses indicated that fertility had been reduced during exposure. Ratios of observed to expected births or standardized fertility ratios (SFRs) were computed for reproductive experience at parities of 1 or greater. The SFR for the period at risk from

DBCP exposure (SFR = 0.63) was significantly lower than those derived from the entire not-at-risk period (SFR = 1.21) or the portion related to nonexposed employment at the plant preceding exposure (SFR = 1.33). Significant reductions would have been evident at least 18 years prior to the year in which the histories were obtained. The effect on fertility seems to have been greatest during the initial period of DBCP production. Most fertility reduction occurred after 3.5 years of exposure. Fertility returned to normal following cessation of exposure (SFR = 1.18), although it appeared to remain subnormal for about two years.

Glass et al (1979) examined male pesticide applicators who worked with the nematocide dibromochloropropane (DBCP) to determine the possible testicular toxicity from this exposure. Infertility and azoospermia which were first noted among factory workers exposed to DBCP were not observed among the applicators. Sperm count depression, however, was associated with the duration of exposure in the current year but not with exposure in past years. The extent of exposure to DBCP in the current year was also associated with an elevation of serum follicle stimulating hormone (FSH) but not of luteinizing hormone (LH). Sperm count depression was limited to applicators involved in irrigation setup work and in the calibration of equipment. These results suggest that the testicular toxicity of DBCP for men may occur in a shorter period than was previously reported, that the effect may be reversible in men with mild sperm count depression, and that public health measures might be directed at controlling specific application techniques.

Glass (1980) in a letter to the Editor expressed the opinion that some of the conclusions stated in an earlier published study by Glass et al. were misleading and that others were inappropriate in a report of an investigation of an occupational hazard. One of them was a co-author of the article in question. The other (D.W.) was the principal investigator in the study of formulating plant workers which first showed dibromochloropropane to be a testicular toxin in man. Glass et al. stated that statistically significant sperm count depression was found only

in the group of men exposed to DBCP for two months or more in the current year. This conclusion is based on the results of analysis of variance of the mean log sperm count of the various groups tested. Elsewhere they said that "the frequency distribution of sperm counts in a group has proven to be the clinical test most sensitive..." but there is no indication that such a test was employed. Using cumulative frequency graphs they have plotted the data from different groups of applicators in the study and compared them to a control group examined by Milby and Whorton . The controls consisted of 90 workers from three chemical plants not exposed to any known testicular toxins. The same laboratory performed the sperm counts for both the Glass study and Milby and Whorton during the same six month period.

In evaluating biological data, one must also examine trends as well as statistical significance. In this study, while the 1 day to 2 weeks exposure group is not significantly different from the reference group, they are obviously not the same as the control. In fact they are more similar to the other exposed groups. In the present case, i.e., examination of the group means of the log of sperm counts and the use of analysis of variance, Glass et al. found a statistically significant depression only in the group exposed longer than 2 months. In stating this finding there is a clear implication that there is no effect on those exposed less than 2 months. Agencies responsible for occupational safety are likely on reading such a statement to make incorrect decisions. Examination of the frequency distribution of sperm counts, however, shows that briefer periods of exposure appear to have a distinct effect. This finding assumes a greatly increased importance in the presence of a clear dose-response relationship. One aspect of the DBCP question that is perhaps insufficiently emphasized by Glass et al. is the fact that the main health concern about this compound is its carcinogenicity rather than its gonadal toxicity. Two more points in the conclusion reached by Glass et al. deserve comment. One is the presumed reversibility of the sperm count depression caused by DBCP. While it seems likely that the relatively mild depressions of short duration are reversible, one of us (D.W.) in following the course of several workers with

azoospermia after long exposure has found that the condition appears to be permanent in almost all cases. A final point is the question of "clinical infertility." It seems obvious that the 15 applicators with sperm counts of 10 million or less (and certainly the six men with counts of one million or less) were not fertile, regardless of their past ability to produce children. To state, solely on the basis of questionnaire answers concerning fertility, that "infertility is not a problem in this group" is clearly misleading. A couple must have attempted unsuccessfully to have children for at least one year before the term clinical infertility can be applied.

Whorton and Meyer (1984) present data from 861 men who have participated in 14 separate occupational studies on testicular function. This population represents the largest series taken from occupational studies. The mean and median sperm counts were 107.1 and 83.0 million/ml of semen, respectively. The percentage of men with sperm counts < 20 million/ml of semen was 8.7%. No significant differences were noted for age or race.

Wyrobek et al (1981) studied a group of workers who previously had been chronically exposed to the broad-spectrum insecticide, carbaryl. They found a "marginally significant" increase in sperm abnormalities among subjects compared to controls, but their controls were all newly employed workmen and were probably much younger than those in the test group. In addition to those exposed to carbaryl, workmen occupationally exposed to the pesticides chlordecone and dibromochloropropane also manifested abnormalities of spermatozoa. However, human epidemiological studies have not established any temporal or spatial association between pesticide manufacture and birth defects.

Wyrobek et al (1981) collected semen from 50 men occupationally exposed to carbaryl (1-napthyl methyl carbamate) in a production plant for durations of 1 to 18 years and compared to semen from a control group of 34 unexposed, newly-hired workers. Employment, fertility, health, personal data, and blood samples were collected for each individual. Semen samples were analyzed

for changes in sperm count, morphology, and frequency of sperm carrying double fluorescent bodies. As a group, the exposed workers showed a significantly higher proportion of sperm with abnormal head shapes than did the control group ($p < 0.005$). Age, smoking habits, and medical problems did not appear to affect this result. This finding appears to be limited to men working in the production area at the time of sampling. Sperm count and YFF did not show similar differences, which may be because they are known to be statistically less sensitive to small changes. Formerly exposed workers (away from carbaryl for an average of 6.3 years) showed a marginally significant elevation in sperm abnormalities compared to controls ($p < .05$ one-tailed statistical analyses) suggesting that the increase in abnormal morphology may not be reversible. However, the question of reversibility is sensitive to confounding factors and small sample sizes and, therefore, requires further study. With these data a definitive link between carbaryl exposure and human seminal defects cannot be established. Although a distinct effect on sperm morphology was seen in the exposed group, the increases in sperm shape abnormalities were not related to exposure dose (estimated by number of years on the job or job classification during the year prior to semen collection). Inexplicably, the increases in sperm abnormalities were seen primarily in currently exposed men who had worked with carbaryl for less than approximately 6 years. These findings suggest the need for further study since other workplace-related factor(s) may be responsible for the elevated sperm abnormalities seen in this study.

Sas and Szoulosi (1972) investigated the effect of long-term driving upon spermiogenesis in 2984 patients, including 281 professional drivers. The incidence of pathospermia was significantly increased among the 281 occupational drivers as compared to other professionals. The ratio of severe pathospermia was increased in proportion to the number of years of driving. The deterioration of spermiogenesis was mild among car drivers, but was severe in agricultural-industrial hard machinery and farm equipment drivers. There was a higher

incidence of impaired fertility in drivers as compared to other professionals.

## Adverse Reproductive Events

### Spontaneous Abortion

Hemminki et al (1980) used a hospital discharge registry covering all general hospitals in Finland in the study of spontaneous abortions. Spontaneous abortions were analysed by the women's occupation and socio-economic class for 1973-75 inclusive. The risk of spontaneous abortion increased from social class 1 to 4 by about 50%. The occupational groups with an increased frequency of spontaneous abortions included industrial and construction work, agriculture, forestry and fishing, sales transport and communication, services, and students and trainees. Decreased frequency of spontaneous abortions was noted among housewives, and in managerial and clerical occupations. The results suggest that socio-economic factors contribute to the rate of spontaneous abortions analogous to their known adverse effects on pre-term birth, birth weight and perinatal mortality.

Saxena et al (1980) investigated premature labour and abortion possibly due to the high concentration of organochlorine pesticides. Considerably higher amounts of organochlorine pesticide residues have been detected by gas liquid chromatography in the circulating blood and placental tissue of the women undergoing abortion or premature labour as compared with pregnant women in full term labour. The differences are highly significant for all pesticides estimated.

Hemminki et al (1980) analyzed childhood cancer, malformations, and spontaneous abortions in Finland according to the parents' occupations. Children of women working in the food industry and farming and of men working in motor vehicle driving and farming appeared to have an elevated risk of cancer. Women in industrial and construction occupations had an increased risk

of having malformed children and spontaneous abortions.

Roan et al (1984) presented information on families engaged in Agricultural Aviation (314) and cooperating sibling families, not occupationally exposed to pesticides (178) who responded to a questionnaire, on their general health status and pregnancy outcomes. These two groups were comparable in age, height, weight, and years of education. Statistical evaluation confirmed the null hypothesis with respect to total pregnancies, number of male or female children, spontaneous abortions, and birth defects.

Heidam (1984) conducted an investigation to test the hypothesis that exposure of pregnant women to chemicals increases the risk of spontaneous abortion. The chemical risk factors under study to which dental assistants, factory workers, painters, and gardening workers were exposed were nitrous oxide, inorganic mercury, organic solvents, and pesticides. The study was carried out within the Danish county of Funen. It included all dental assistants employed in private or public dentistry. A comparable reference group was made up by employees less exposed to chemicals. Further study groups included all women painters within the county, women factory workers from selected factories, and about 50% of the women gardening workers within the county. Shop assistants and packers formed their control group. Information was obtained through a postal questionnaire study in May 1980 and from hospital records. Only among factory workers and painters was the odds ratio of spontaneous abortion found to be significantly increased. Neither among these women nor among dental assistants and gardening workers, however, was the reported exposure to any single chemical during pregnancy associated with a significantly increased odds ratio of spontaneous abortion.

## Prematurity

Wasserman et al (1982) assessed some organochlorine compounds (OCC), DDT and metabolites, y-HCH, dieldrin, heptachlor

epoxide and polychlorinated biphenyls in the serum of 17 women with premature delivery (PD) and 10 women with normal, third-trimester pregnancy. Out of 17 cases of PD, 8 cases were associated with high PCB serum levels (128.0 ppb versus 19.25 ppb in the control group), and 5 cases with high DDT serum levels (119.6 ppb versus 26.5 ppb in the control group). Two of the cases with high PCB serum levels also had high total DDt serum levels. The 5 cases with high total DDT serum levels also had high y-HCH and heptachlor epoxide serum levels and 4 out of these 5 cases also had high dieldrin serum levels. The higher chlorinated PCB isomers constituted a higher percentage of total PCBs in the study group in comparison with the control group (about 30% versus 8.94%). At the same time, the percentage of total o.p'-DDT was unusually high (50% of total DDT in the study group versus 30% in the control group). The possible role of the relatively high serum levels of the organochlorine compounds assessed in this study, in the occurrence of PD, is discussed.

## Stillbirths and Neonatal Death

Saxena et al (1983) quantified hexachlorocyclohexane aldrin, p,p'-DDt, p,p'-DDD, and p,p'-DDE in specimens of maternal blood, placenta, and umbilical-cord blood from women experiencing stillbirth and live birth. Specimens of stillbirth cases were found to have higher organochlorine insecticide contents as compared to matched controls. The levels of aldrin and p,p'-DDT in all the three specimens of stillbirth cases were found to differ significantly from the controls. A significant correlation was noticed between maternal blood and placenta for total HCH, lindane ( -HCH_, and p,p'-DDT while in the cases of maternal blood and umbilical-cord blood, aldrin, p,p'-DDT, and total DDT were found to be significantly correlated.

## Congenital Malformations

Klingberg et al (1983) observed that population monitoring

of birth defects provides a means for detecting relative changes in their frequency. Many varied systems have been developed throughout the world since the thalidomide tragedy of the early 1960s. Although it is difficult to pinpoint specific teratogenic agents based on rises in rates of a particular defect or a constellation of defects, monitoring systems can provide clues for hypothesis testing in epidemiological investigations. International coordination of efforts in this area resulted in the founding of the International Clearinghouse for Birth Defects Monitoring Systems (ICBCMS) IN947. They will describe the functions and basic requirments of monitoring sysems in general, and look at the development and activities of the ICBDMS. A review of known and suspected environmental teratogenic agents (e.g., chemical, habitual, biological, physical, and nutritional) is also presented.

Klingberg and Papier (1979) presented a review of the field of human teratoepidemiology - the epidemiology of congenital malformations - along with a discussion of the importance of international collaboration in monitoring congenital malformations. Studies implicating various environmental teratogens such as drugs, industrial and agricultural chemicals, intrauterine infections, radiation and nutritional factors are discussed at some length as well as problems encountered in detecting human teratogenic agents.

Williams et al (1981) assessed the risks of congenital anomalies in the Holland Marsh and surrounding areas. This feasibility study was called for when Dr. Eric Holowaty found an unusually high risk of congenital anomalies in the area including the Holland Marsh for the years 1975 to 1978. To determine if a community health survey was necessary, there was a review of 13,594 notifications of live births and stillbirths from 1973 to 1979 for the township of West Gwillimbury (including Bradford and most of the marsh areas); the peripheral townships of King, Tecumseth, East Gwillimbury, Georgina, and Innisfil; and, Barrie and Newmarket were used as control communities.

In the findings, they did find the rates of congenital anomalies and stillbirths were unusually high for West

Gwillimbury in comparison to the other areas for the time period 1975 to 1978, confirming Dr. Holowaty's findings. The rates of congenital anomalies and stillbirths were not high during the months of the growing season.

If there is additional evidence of significant clusterings of congenital anomalies, or if more direct linkages are made by health professionals between poor birth outcomes and specific risk factors, then an additional study is warranted.

The Disease Control and Epidemiology Service, Public Health Branch of the Ministry of Health did a Study of Selected Reproductive Outcomes Among Residents of Simcoe County, Ontario, 1975-1982. A review of data reflecting reproductive health was undertaken to examine the possibility of potential adverse health effects of aerial pesticide spraying in the vicinity of Tiny township Simcoe county, Ontario, a community of 7,170 population in 1981. Data on congenital anomalies detected during the first year of life for the years 1975-1982, stillbirths 1970-1982, and spontaneous abortions (miscarriages) 1975-1983 were examined. These indicators of reproductive experience among Simcoe county residents were compared to those of the province as a whole using standardized reproductive ratios (similar to standardized mortality ratios). The number of stillbirths in Simcoe county was within expected limits, with the exception of the single year 1977, when a higher than expected number of stillbirths occurred. An expected rate of occurrence of congenital anomalies was experienced in the county, except for an increased incidence of hydrocephaly in the combined time period 1975-1979 and an elevated incidence of anencephaly (total number = 4) among births to Simcoe county residents in 1982. Spontaneous abortions among residents of the county remained well within expected limits for the years studied.

Kurppa et al (1983) performed a screening for occupational exposures and congenital malformations and reported preliminary results from a nationwide case-referent study. Since 1976 the Finnish matched-pair Register of Congenital Malformations has been linked to a special project which screens for associations

between selected congenital malformations and chemical and physical exposures during early pregnancy. Case mothers and their referents are personally interviewed. Exposure data are quantitated blindly by a team of industrial hygienists and occupational health experts. An analysis of data from 1,047 pairs is now underway. The pairs consist of 289 defects of the central nervous system, 421 orofacial clefts, 200 selected structural malformations of the skeleton, and 137 selected cardiovascular defects. Exposure to organic solvents was associated with defects of the central nervous system in the initial two-year material. However this association was no longer detectable during the following three-year period. More pairs must be gathered before a reasonable judgment regarding the teratogenic potential of solvents becomes possible.

Gibson et al (1983) obtained data on exposure of 10,879 pregnant women to various household and agricultural chemicals by interview; 6,267 of these women were seen both antenatally and postnatally, enabling a genuine prospective study of the association between chemical exposure and congenital abnormalities in the infant. The remaining 4,612 women were privately booked and were first seen postnatally. Statistical analysis of the 2 groups revealed a strong association of malformations of chemical exposure in both groups, even after other known risk factors were taken into account.

Gordon and Shy (1981) conducted a case-control study utilizing vital records and ecologic, surrogate exposure measures in Iowa and Michigan. The study hypothesis anticipated an excess risk of clefts among fetuses exposed during the peak agricultural chemical use period (April through November) coincident with their first trimester of gestation. To examine this hypothesis, multiple regression techniques were used to aid identification of potential confounders; additional analyses, stratified on the potential confounders, were performed using two chemical exposure indices. The major findings of these analyses suggest: (1) an agricultural chemical effect (using multiple exposure index) controlling for season of conception; (2) no independent effect of season of conception (thus the null hypothesis is not

rejected); and (3) little chemical/season interaction. These results imply that if exposures to agricultural chemicals are, in fact, risk factors for clefts, an expanded model that accounts for multiple pesticidal exposures may be more sensitive than consideration of season of exposure, as originally hypothesized.

Smith et al (1982) conducted a survey of professional New Zealand 2,4,5-T sprayers and a comparison group of agricultural contractors with a total of 989 respondents. The numbers of births, congenital defects, and miscarriages were identified from 1969 to 1980 by a postal questionnaire. Each pregnancy outcome was classified according to whether or not the father sprayed 2,4,5-T during the year of the pregnancy outcome, or the previous year. The relative risk estimates of 1.19 for congenital defects, and 0.89 for miscarriages, were not statistically significant. These results are reassuring as far as male professional 2,4,5-T sprayers are concerned. In addition,the extent of exposure of their wives from helping with spray activities, and from washing contaminated clothes, has not had a detectable reproductive effect.

Brogan et al (1980) observed that the incidence of cleft lip and/or palate (CLP(P)) in Western Australia has been ascertained from multiple sources and related to the State birth- rate. In Western Australia roughly two-thirds of the population live in Perth, the State capital, and one-third live in the country area. Normally the incidence of CLP(P) relates to the numbers born in each area. In 1978 we noted that the incidence of CLP in the country appeared to be significantly higher than expected. The total incidence of CLP(P) in Western Australia has declined during this period, there has been no significant change in the seasonal incidence ( $t = 5.94$, $p < 0.01$); the combined incidences from spring and summer conceptions are significantly higher than those for winter and autumn conceptions ( $t = 3.91$, $p < 0.001$). Thus it can be concluded that Western Australian children with cleft defects have a significantly higher chance of having been conceived in spring and summer than in autumn and winter. The number of cases of CLP(P) occurring in Western Australia is

relatively small, and the surveys have been retrospective. However, the pattern of potential causative factors reported has changed, a trend for these malformations to be associated with exposure to insecticides and herbicides seems possible.

Smith et al (1981) compared reproductive outcomes among New Zealand chemical applicators using 2,4,5-T and other pesticides with those of agricultural contractors by means of a postal questionnaire survey. The overall response rate of 86 percent yielded 459 married chemical applicators and 422 married agricultural contractors. Rates of congenital defects, stillbirths, and miscarriages among the 1172 chemical applicator births were compared with the rates among the 1122 agricultural contractor births. No significant differences were found and the rates of congenital defects of 20 per 1000 births for the chemical applicators and 16 per 1000 births for the agricultural contractors were close to those reported in other New Zealand studies.

Lipson (1983) cited two major studies on this topic, both incidentally, conducted in Australasia. The first study was a large, independent investigation of the offspring of Australian Vietnam veterans. The second study, conducted in New Zealand, examined the handlers of 2,4,5-T. These men are usually farmers, who often mix the chemicals with their bare arms, and do not wear protective clothing. This controlled study was carried out over a period during which dioxin was a common contaminant in herbicides. It, too, failed to demonstrate an adverse effect on the offspring of men exposed to 2,4,5-T.

However, Balarajan and McDowall (1983) examined the father's occupation recorded as part of the Office of Population Censuses and Surveys' congenital malformation monitoring programme in England and Wales for 1974-79. Occupations likely to involve the handling of herbicides were taken to be units 002-006 from the OPCS Classification of Occupations (1970). The malformations studied were those suggested as being associated with 2,4,5-T. They calculated malformation ratios for these occupation units by comparing the number of notified malformations in a unit to that

expected on the basis of rates for all fathers with an occupation stated on the malformation notifications. Rates were derived from comparisons with the number of total births (live and still) registered in England and Wales to fathers in the respective occupations, but the results are presented as ratios due to under-reporting of occupations at malformation notification. The results are shown in the table.

SELECTED MALFORMATION RATIOS BY FATHER'S OCCUPATION FOR YEARS 1974-79: ENGLAND AND WALES

| | Malformation ratio (and no of cases for: | | |
|---|---|---|---|
| Occupation Unit | Spina bifida | Anencephaly | Cleft lip and/or palate |
| 002: farmers farm managers market gardeners | 85(34) | 94(23) | 107(41) |
| 003: agricultural workers* | 128(38) | 100(18) | 127(36) |
| 004: agricultural machinery drivers | 43(2) | 105(3) | 112(5) |
| 005: gardeners or groundsmen | 123(19) | 117(11) | 142(21) |
| 006: foresters or woodmen | 63(2) | 103(2) | 164(5) |
| | 100 | 100 | 100 |

Malformation ratios for all notifications with father's occupation given = 100.

*Not elsewhere classified

Malformation ratios for facial clefts were consistently high. "Gardeners and groundsmen" (005) showed increased ratios for spina bifida, anencephaly, and facial clefts, and "agricultural workers" for spina bifida and facial clefts. The process of self-selection into occupation is by itself unlikely to lead to a genetic predisposition sufficient to explain the ratios for clefts in all the units studied. Also those classified in these units would have varying exposure to many agents besides phenoxyacids and related compounds.

Golding and Slatten (1983) have looked at evidence from three population studies where occupation histories of both cases and the population at risk were taken from birth (or stillbirth) certificates. Information has been collected for all births to

women resident in Oxfordshire and West Berkshire since 1965, by the Oxford Record Linkage Study. Of all births, 3.7% had fathers who worked in agriculture, horticulture, or forestry. Specific projects to identify all cases of anencephalus, spina bifida, and cleft lip/palate have been carried out for births in the years 1965-72, 1965-72, 1965-74 respectively. For this population, the relative risk to infants of fathers in agricultural, gardening, and forestry as opposed to all other infants was 1.2 (based on 8 of 177 cases) for anencephaly, 0.8 (7 of 238 cases) for spina bifida, and 0.9 (8 0f 240 cases) for clefts. There were only 2 gardeners involved, both in the cleft group.

Further data were available for 555 anencephalics born in England and Wales in 1969. They were compared with 2200 controls matched for maternal age, parity, and region. Half the controls were stillbirths without anencephaly and half livebirths. There were 12 anencephalics with fathers who were farmers or farm-workers, compared with 47 controls (relative risk 1.0) and 4 gardeners compared with 7 controls (relative risk 2.3). None of the results was significant. There is little to confirm that there were slightly more infants than expected born with each malformation to men with occupations in the agricultural industry in the years before the study of Balarajan and McDowell. The herbicide 2,4,5-T was first used in 1944 and it was used fairly consistently from the late 1940s onwards, mainly for clearing scrubland. There is little to suggest that it has a teratogenic effect, from the indirect evidence presented here.

## Postnatal Manifestations

Casey and Collie (1984) describe extreme developmental delay and unusual phenotypic abnormalities in a child whose parents had prolonged and extreme exposure to 2.4-D before and during pregnancy. Both parents participated in forestry spraying of an herbicide consisting of 2,4-D and 2,4-D amine. A spray aerosol bottle was used, and the chemical was sprayed into hatchet marks in the trees. This spraying occurred 6 days per week, approximately 7 hours per day, from 6 months prior to conception until the pregnancy was confirmed approximately 5 weeks after the

mother's last menstrual period. No protective masks were worn, and the chemical was frequently inhaled. Long sleeves, pants, and rubber gloves were almost always used. The father continued spraying throughout the pregnancy, and the mother laundered his work clothes during this time.

This patient had severe mental retardation and a constellation of phenotypic abnormalities not specific for any known genetic disorder. Although the cause in a significant percentage of children with severe mental retardation is undiagnosed, it is believed that severe-profound retardation in the presence of multiple major and minor phenotypic abnormalities likely are attributable to prenatal factors. They believe that her multiple malformations and severe mental retardation may be related to prolonged parental exposure to 2,4-D and 2,4-D amine. Studies with microorganisms, plants, and the fruit fly have been somewhat conflicting, but they suggest the mutagenic potential of 2,4-D. Teratogenic effects have also been reported in mammalian species after exposure to 2,4-D and 2,4,5-T, a close chemical relative. Both parents of our patient had extreme and prolonged respiratory and cutaneous exposure to 2,4-D, probably significantly more severe and prolonged than that experienced in aerial spraying or in those industrial accidents investigated previously, which have not confirmed the association of phenoxyacids with birth deformities. Such extensive exposure may be required for 2,4-D to have teratogenic or mutagenic effects, and it may have these effects by both parents.

Crampton and Rogers (1983) reported that pre-natal exposure of rats to 2,4,5-T has long-term effects on behavior. A test for novelty responding detects abnormalities after exposure to a single dose as low as 6 mg/kg on day 8 of gestation. This is well below doses reported to be morphologically teratogenic, and raises concern for human exposure.

Bulger and Kupfer (1983) discussed the estrogenic action of DDT analogs, among these methoxychlor. Emphasis is placed on investigations of estrogenic properties of DDT derivatives, their long-term effects on reproductive processes, and their mechanism

of action. Kepone is discussed briefly as an example of another structural class of insecticides with estrogenic activity.

Eckenhausen et al (1981) obtained samples of blood from Dutch mothers and their babies throughout the perinatal period and analyzed them by gas-liquid chromatography with electron-capture detection for a range of organochlorine pesticides. Organochlorine concentrations in the blood of breast or bottle-fed babies were not significantly different. Differences in organochlorine concentrations in blood between mothers who had "slimmed" and those who had not were small, but it must be noted that there were few slimming mothers in their sample. Twelve to 21% and 36-61% of the estimated daily intake of dieldrin and DDT, respectively, by mothers may be eliminated by lactation. The placenta restricts the transmission of organochlorine pesticides to the fetus to some extent. The very low concentrations of organochlorine in fetal blood prevented a study of the comparative metabolism in mothers and babies.

Grady and Kitay (1978) observed that prenatal exposure to pesticides of three different classes initiated persistent postnatal endocrine dysfunction. Adrenal function and hepatic metabolism of corticosterone were studied in adult hybrid mice exposed during development to either an organophosphate (Diazinon), a carbamate (Carbofuran), or an organochlorine (Chlordane). Animals were expoosed to relatively low levels of the toxins in utero and neonatally via the mothers' milk. Exposure to lower doses of the anticholinesterase compounds, Diazinon or Carbofuran, resulted in impairment of hepatic metabolism of corticosterone in vitro due to a loss in reductive capacity per unit liver weight. Plasma levels of corticosterone were also elevated in these animals, but without a concomitant increase in adrenal steroidogenesis in vitro. The effects of exposure to Chlordane were more complex. In male animals, exposure to lower doses of chlordane resulted in an increase in plasma corticosterone levels without an apparent increase in hepatic metabolism of corticosterone or adrenal steroidogenesis. In contrast, side-chain metabolism of corticosterone was decreased in female mice exposed to Chlordane. Similar effects

on pituitary-adrenal function were not evident for the offspring of mice exposed to higher doses of the toxins. Possible mechanisms for this non-linear dose-response are discussed.

D'Ercole et al (1976) noted that pregnant women in a rural agricultural area were found to have levels of residues of chlorinated hydrocarbon insecticides in their serum which were comparable to those found in occupationally exposed men. Cord blood of offspring also had significant residue levels. Residues were higher in blacks and in mothers living in rural areas where exposure was more intense. In newborns no signs or symptoms compatible with acute chlorinated hydrocarbon poisoning were found. Despite the lack of DDT use during most of the study period, over 90% of the mothers, 84% of the black newborns, and 45% of the white newborns demonstrated evidence of recent DDT exposure.

## Strategies for Prevention

Infante and Tsongas (1983) observed that although some attention has recently been given to the study of occupational reproductive hazards, little is known about measures being taken to prevent exposure to substances having the potential to cause such problems. In the past, OSHA has promulgated a standard to lower the permissible exposure level to a reproductive toxin as the major focus only after experimental evidence was confirmed in humans. The method of selection of appropriate substitutes is also cause for concern. A chemical known to cause testicular atrophy, cancer, and gene mutations in subhuman test systems and to cause sterility in male workers was replaced with a substance known from experimental studies to cause testicular toxicity, cancer of multiple sites, and gene mutations. Experimental test results need to be addressed from the standpoint of determining presumptive risk to humans. A scheme for setting priorities for reduction of exposure or for consideration of regulation of occupational reproductive hazards also needs to be developed. A policy addressing occupational reproductive hazards may serve as

a stimulus for protecting workers from these hazards and for improving scientific research protocols.

Hatcher and White (1984) addressed the 1st, 2nd, 3rd and (partially) the 5th Terms of Reference of the Task Force on Chemicals in the Environment and Human Reproductive Problems in New Brunswick. The focus was on trends and patterns of adverse reproductive outcomes, assessments of the toxicology and regulation of selected pesticides, and the development of an environmental chemical data base for New Brunswick. In view of their relative frequency and plausible environmental hypotheses, particular attention has been given to the occurrence of neural tube defects (anencephaly, spina bifida) and facial clefts. In addition, renal agenesis and the category "all anomalies" have been closely studied, as have stillbirths and preterm births. Seven recommendations pertaining to toxicology assessments are made:

- Canadian criteria for the performance of toxicology studies
- Access to essential regulatory information by government appointed inquiries
- Periodic regulatory review of licensed chemicals
- A product and environmental monitoring program
- An analytical chemistry program
- Use of primates in studies of teratogenicity and and reproduction toxicology
- A maximum allowable contaminant level of 2,4,5-T

It is clear from this review of reproductive hazards and farm work that further research is urgently required in Ontario. The lack of a comprehensive surveillance system for monitoring of adverse reproductive outcomes inhibits the preliminary explorations of events necessary before large scale epidemiological studies can be initiated. Protection of the health of the wanted unborn is such a high social priority that immediate action is warranted.

# CHAPTER SIX

# NEUROLOGICAL DISORDERS AND FARM WORK

## Acute Neurotoxicity

### Organophosphates

Hirshberg and Lerman (1984) discussed clinical problems in organophosphate insecticide poisoning. A computerized medical information system has been constructed, which contains clinical data from 236 case records of organophosphate and carbamate insecticides poisoning in Israel. A computer program was used to retrieve, analyze, and cross-tabulate data contained in 162 variables per patient. Clinical criteria were used to distinguish mild (66%) from moderate (19%) and severe (15%) cases. The majority of exposures were occupational (58%), whereas the rest were accidental (31%) or suicidal (11%). Parathion was the toxic compound most frequently involved (153 cases). Grouping signs and symptoms according to the cholinergic synapse systems showed peripheral muscarinic signs to be the most prevalent (92%) of cases, whereas involvement of all three synapse systems was rare (17%). Listing individual symptoms emphasized the high prevalence of nonspecific symptoms such as vomiting (142 cases) and abdominal pain (115 cases). The mean atropine dose given to adult patients during the first 24 hours after poisoning ranged from 6.0 +/- 0.7 mg in mild cases to 49.8 +/- 4.5 mg in severe cases. Evaluation of clinical decision making was demonstrated through analysis of the guidelines used by physicians to gauge atropine administration. Five of the 18 fatalities were delayed deaths, one of which was due to a polymorphous ventricular arrhythmia. The same arrhythmia occurred also in four nonfatal cases. Other delayed effects included nonspecific EEG changes and neuropsychiatric symptoms. Matching individual cases with comparable cases in the data bank was demonstrated, using a previously published case report.

Kashyap et al (1984) evaluated the clinical manifestations and cholinesterase (ChE) activity before and after 2 weeks of

exposure to phorate in 40 male formulators. The 2 week's exposure reveal signs and symptoms of toxicity in 60% of the formulators. Gastrointestinal symptoms and lowering of heart rate (bradycardia) were more prominent as compared to the neurological symptoms. A significant depression in plasma ChE activity was observed at the end of 1st week (55%) and 2nd week (71%) as compared to the respective pre-exposure values. A recovery up to 79% of the pre-exposure activity of this enzyme was noticed 10 days after cessation of the above exposure.

Sterling (1983) reviewed poisoning by cholinesterase-inhibiting insecticides. The therapeutic and toxic actions of these agents are due primarily to inhibition of the breakdown of acetylcholine, which allows acetylcholine to accumulate at cholinergic receptors throughout the peripheral and central nervous systems. The management of toxicity from these agents is important because of their easy accessibility as agricultural and garden insecticides. He describes the clinical diagnosis and treatment of poisoning by the cholinesterase-inhibitor type of insecticides.

Whorton and Obrinsky (1983) reported on exposure to 2 organophosphate pesticides which occurred when entry into a cauliflower field was permitted 4 hours after application of highly toxic chemicals. It resulted in acute illness of mild to moderate degree in 19 farm workers, including 3 children and 1 pregnant woman. There were no fatalities. Two to three months were required for recovery from major symptoms and return to normal acetylcholinesterase levels. An exception was the persistence of eye symptoms in the majority 4 months after the day of exposure.

Jusic and Jurenic (1980) evaluated electromyographic neuromuscular synapse testing and neurological examination for early detection of organophosphorous pesticides intoxication. Two groups of healthy agricultural workers and one group of healthy spraymen were exposed to various organophosphorous pesticides of different intensities. An additional group of

nonexposed agricultural workers was also analyzed for comparative purposes. Before and during exposure, cholinesterase activity was determined. Personal, occupational, medical, and neurological case histories were taken; during the same session electromyographic synapse testing was performed and neurological information was recorded. No significant difference between exposed groups and the control group was found. The electrically evoked muscle potential series in exposed workers remained as constant as those recorded for the control group. The frequency of different types of amplitude changes was the same in exposed groups and in the control group. Neurological records showed no significant deviations from normal for exposed workers.

de Reuck et al (1979) presented the clinico-pathologic findings in two patients with an acute organophosphorus intoxication who died from an atypical central neurologic disorder.

Case 1 was an 28-year-old man, with a previous history of chronic alcoholism, was admitted to the intensive care department, approximately 5 hours after ingestion of an unknown amount of alcohol, chlordiazepoxide and trichlornate, an organophosphorus cholinesterase inhibitor, used as an insecticide. After an initial improvement of the symptoms of cholinesterase poisoning, the neurologic state of the patient became suddenly worse on the 4th day after admission. He developed high fever, bronchopneumonia, gastric bleeding and acidosis. His consciousness decreased and the four extremities became hypertonic with excessively brisk and clonic tendon reflexes, but without Babinski signs. He became more and more deeply comatose and after an attack of gram-negative sepsis by Klebsiella Pneumoniae he died 20 days after admission. The necropsy revealed massive gastro-intestinal bleeding, due to three gastric ulcers, severe bronchopneumonia and pleuritis, acute tubular necrosis and a fatty liver.

Case 2 was an unconscious 50-year-old man, with a previous history of recurrent depressions who was admitted to the intensive care department approximately 6 hours after ingestion of an unknown amount of dimethoate, an organosphosphorus insecticide. Sixteen hours after admission he developed

respiratory difficulties, a short episode of hypotension, bradycardia and cardiac arrest, due to bronchial obstruction due to abundant secretions. On the third day of hospitalisation dopamine had to be administered because of the occurrence of shock and after a second cardiac arrest the patient needed positive and expiratory pressure ventilation for bilateral lung infiltrations with low $PO_2$. At that time the plasma cholinesterase activity had normalized, but the activity in the red blood cells remained inhibited for almost 90%. The patient remained unconscious. During the next few days the patient became more and more deeply comatose and died on the 9th day of hospitalisation.

Both cases presented, showed clinical signs of a cholinesterase poisoning due to ingestion of an unknown amount of an organophosphorus cholinesterase inhibitor. Both were treated in approximately the same way, and high doses of vitamin B complex were given intravenously. Although the cholinesterase activity in serum and red blood cells was severely inhibited, the clinical evolution at first seemed to be favorable. Besides their acute neurotoxicity, causing central and peripheral signs of cholinergic hyperactivity, some organophosphorus compounds can produce a delayed neurotoxicity, involving peripheral nerves and the posterior columns of the spinal cord. The neuropathologic findings in the cases presented were similar to those observed in severe forms of Wernicke's encephalopathy. The similarity of the neuropathologic findings with Wernicke's encephalopathy in the cases presented suggests that the 'biochemical lesion' is related to the thiamine metabolism.

Stalberg et al (1978) presented neurophysiological investigations and determinations of cholinesterase activity on plasma and erythrocytes on 11 Swedish spraymen exposed to bromophos, diazinon, dursbane, and malathion. Plasma cholinesterase activity was significantly reduced after work, while erythrocyte cholinesterase activity was unchanged. In none of the workers with a decreased plasma cholinesterase activity after work could any related acute neuromuscular disturbance be detected when the men were tested with repetitive nerve

stimulation and with single fiber electromyography. Signs of subclinical neuropathy were present as a slight reduction in sensory conduction velocity and increased fiber density in some workers.

Spear et al (1977) observed that during June 1975, three poisoning incidents occurred among agricultural fieldworkers in Tulane County, Calif. These incidents have been attributed to exposure to residues of ethyl parathion on the foliage of orange trees and in the soil on the grove floor. These episodes are the most recent in a long history of such incidents in California and are the most thoroughly investigated since the outbreak reported by Milby et al in peach orchards in central California in 1963. These most recent investigations were carried out by three state agencies and two county agencies as well as one federal and two university research groups. It is our purpose to summarize the factors which contributed to these episodes. As well as to interpret these events in the light of recent research results which implicate paraoxon as the principal toxic constituent of weathered parathion residues in this region.

Kraus et al (1977) monitored the physiologic response of 21 male agricultural field workers exposed to foliage-borne Guthion residues during routine peach-thinning operations in a northern California orchard. Surveillance included daily venipuncture and urine collection to determine whole blood cholinesterase (CHE) activity and level of dialkylphosphate excretion for 3 baseline (nonexposed) and 5 normal work days. Foliage samples were obtained to measure dislodgeable and total Guthion residues. A decrease in group mean CHE activity by 15% over the surveillance period was found. Apart from one worker who showed a consistent decrease in CHE activity, reaching a maximum of 30% below baseline at the end of the work week, daily changes in individual CHE activity were erratic. Group-mean dialkylphosphate excretion levels provided a semiquantitative indication of exposure to Guthion. Medical examination before and after the exposure period revealed an absence of clinical signs of organophosphate intoxication.

Levin et al (1976) assessed psychiatric manifestations of exposure in workers less substantially exposed to organophosphate compounds and showing no obvious signs of toxicity. Commercial pesticide sprayers and farmers recently exposed to organophosphate agents were compared to control subjects on personality tests, a structured interview, and cholinesterase level. The commercial sprayers but not the exposed farmers showed elevated levels of anxiety and lower plasma cholinesterase than control subjects. Assessment of other behavioral manifestations and red blood cell cholinesterase failed to disclose other group differences. These findings are viewed as tentative until confirmed by additional study, but they point to the possibility that organophosphate compounds may produce subtle defects in workers who are not obviously toxic. The findings do not justify public alarm but do suggest an area warranting more systematic and definitive investigation.

Rodnitzky et al (1975) tested the hypothesis that similar neurobehavioral abnormalities might be present in mild degree in workers chronically exposed to organophosphate pesticides, 23 such subjects were tested for abnormalities in memory, signal processing, vigilance, language, and proprioceptive feed-back performance. The performance of the exposed workers was not deficient in any of the five measures assessed when compared with the performance of a control group matched for age and educational background. Plasma and red blood cell cholinesterase levels were found to be in the normal range in both exposed and control groups, although plasma levels of exposed subjects were depressed somewhat below control values. Relative resistance of higher nervous system functions to mild chronic organophosphate exposure is suggested by these results.

## Other Pesticides

Miller (1982) reviews the two major classes of pesticidal carbamates: (1) cholinesterase-inhibiting carbamates which include monomethyl- and dimethylcarbamates (used primarily as

insecticides); and (2) non-cholinesterase inhibiting, sulfur containing carbamates, the dithiocarbamates (used primarily as fungisides and herbicides). The dithiocarbamates include four major classes; (a) methyldithiocarbamates, (b) dimethyldithiocarbamates, (c) diethyldithiocarbamates, (d) ethylenebisdithiocarbamates. For the purposes of this review neurotoxicity is defined as any unwanted change in the functional status of the organism which can be characterized in terms of behavioral, neurochemical, electrophysiological, or neuropathological indices. Neurotoxicity associated with methyl- and dimethylcarbamates has been characterized in terms of their reversible cholinesterase-inhibiting properties. The dithiocarbamates can have neurotoxic effects. However, a complete characterization of the neurotoxicity of these compounds has not been attempted. The neurotoxic actions of the dithiocarbamates may be related to their metal-chelating and enzyme-inhibiting properties.

Reich and Spong (1983) describe one of the most costly chemical disasters in the United States involving a small, single-product manufacturer, ironically named Life Science Products Company, which made the pesticide Kepone for Allied Chemical Corporation. Life Science operated only 16 months in 1974 and 1975, in Hopewell, Virginia, yet managed to poison its workers and pollute the environment, causing millions of dollars of damage. The case dramatically demonstrates the links between hazards inside the factory and those outside the factory, and the confused responses of both administrative and judicial systems to a chemical disaster. In the Kepone case, as in other instances of toxic contamination, the victims confronted problems of care, compensation, and clean-up. The case illustrates two major causes of a chemical disaster: organizational pathologies of public bureaucracies, and irresponsible production by private corporations.

Knox et al (1984) reported occupational exposure to fenvalerate, a synthetic pyethroid insecticide. It has been reported to cause paresthesia. An assay was devised in our laboratory for subjective grading of the sensation produced by

the topical application of this compound. The present double-blind study compared human discrimination of topically applied technical fenvalerate, the heavy-ends fraction of fenvalerate, and ethyl alcohol (vehicle). Both forms of fenvalerate showed a statistically significant increase in inducing paresthesia over the vehicle alone. The onset of the cutaneous sensations occurred at one hour, peaked at three to six hours, and lasted approximately 24 hours. Numbness, itching, burning, tingling, and warmth were the most frequently reported sensations. The difference between the two fractions of fenvalerate was not statistically significant.

Tucker and Flannigan (1983) determined through a field survey, the prevalence of cutaneous response to the synthetic pyrethroid fenvalerate; to characterize the cutaneous reaction; and to identify the setting in which it occurs. The methodology involved case studies of selected individuals who had worked extensively with fenvalerate in the delta region of Mississippi and Alabama. All the agricultural workers interviewed and examined had, on some occasion, noted a paresthesia which they associated with exposure to this pyrethroid insecticide. The cutaneous sensation described was a stinging or burning which progressed to numbness in approximately one-third of the exposed workers. The sensation typically began a number of hours after contact, peaked in the evening, and rarely was present the following morning. The intensity of the sensation varied according to the type and extent of exposure. Clinical signs of inflammation such as edema or vesiculation were not apparent. Erythema was present in a limited number of individuals but was not distinguishable from sunburn. Several environmental factors were found to affect the cutaneous sensation associated with fenvalerate exposure.

Hessl and Berman (1982) reported a case of severe peripheral neuropathy after several days of exposure to a pesticide spray containing monosodium methyl arsonate. The clinical manifestations of symmetrical peripheral neuropathy with stocking-glove sensory deficit, decreased position sense,

decreased and absent deep tendon reflexes, and muscle wasting are consistent with those described in other cases of arsenic intoxication. The anemia, leukopenia, and bone marrow changes of dyserythropoiesis in this case are also similar to those previously describaed with arsenic intoxication. The authors discuss the possible contribution of toxicity from exposure to other pesticides.

Grant et al (1980) report on cerebral changes in eight patients who died of paraquat poisoning. These included generalized oedema, haemorrhages (both subependymal and subarachnoid), glial reactions (microglial activity and astrocytic response) and meningeal inflammation. Oedema and haemorrhage were the most consistent and significant findings: they suggest that paraquat may damage the cerebral blood vessels. The distribution of haemorrhages was unusual and resembled that seen in thiamine deficiency.

Sandifer et al (1981) conducted a study of twenty-seven pesticide workers with elevated blood levels of dieldrin (> 15 ppb) involved in a case-control study which included history and physical examination, comprehensive neurological evaluation, laboratory tests, and psychological and psychomotor testing. No clinically important differences were found on history, physical, specialized neurological tests, or laboratory examination. The exposed group showed a statistically significant difference in 5 out of 58 psychological (P) and psychomotor (PM) tests - at least three would be expected by chance ($p < .05$). In only one of these tests was there any significant correlation with dieldrin levels. Even though the exposed group had worse scores than the control group in 47 of 58 P - PM tests, such scores were, with a few exceptions, in the normal range of values. Elevated blood levels of dieldrin encountered in this study do not appear to have any chronic deleterious effects on health, as measured by conventional medical work-up and extensive central nervous system testing.

Gupta (1975) reported on eleven members of a small village community and five domestic animals who developed evidence of

neurotoxicity in the form of myoclonic jerks and major motor seizures on being exposed to chlorinated hydrocarbon group of insecticide (Aldrin and Gamaxin) for a period of 6 to 12 months. Electroencephalographic (EEG) study in six of these cases showed excess of slow waves, spike activity and paroxysmal burst of delta wave abnormality. Both the clinical and EEG features have been demonstrated to be reversible. Diazepam was found to be more effective anticonvulsant compared to phenobarbiton and phenytoin sod in controlling the myoclonic jerks and other minor seizure phenomenon seen in these cases.

## Delayed Neurotoxicity

Lotti et al (1984) reviewed the experimental evidence for organophosphorus-induced delayed polyneuropathy (OPIDP) initiated by the phosphorylation of a protein neurotoxic esterase (NTE) in the nervous system. A second step, the "aging" of the phosphoryl-enzyme complex, is required to produce the toxic effect. The catalytic activity of NTE has been used to develop an in vitro screening test that may distinguish the organophosphorus compounds (OPs) that cause neuropathy from those that do not, thereby providing a means for prevention of OPIDP. Moreover, a biochemical screening test, the determination of NTE activity in blood lymphocytes, may predict the development of OPIDP after acute or chronic exposure to OPs.

Extrapolations from in vitro to in vivo data in humans now seem justifiable and predict which toxic effects are likely to predominate after exposure to a given OP.

Such extrapolations assume that to trigger OPIDP, the same amount of inhibition of NTE is necessary in humans as in the experimental animal. In fatal OP poisoning, measurement of AChE and NTE activities in postmortem tissue would help to build up a data bank for comparison with clinical responses in nonfatal cases.

NTE activity has been found in lymphatic tissues. Measurement of NTE in circulating lymphocytes, therefore, may be a means of evaluating the potential neurotoxic hazard after OP

exposure. Serial measurements of lymphocyte NTE activity soon after acute poisoning with OPs known to cause OPIDP may further characterize the use of this test as predictor for development of OPIDP in humans.

Measurement of lymphocyte NTE has also been used to monitor chronic occupational exposures to OPs known to cause OPIDP. A correlation between the intensity and length of the exposure and the inhibition of lymphocytic NTE was found, but there were no clinical or laboratory signs of peripheral neuropathy. This may have been because the threshold of enzyme inhibition was not reached, or may indicate that the NTE in lymphocytes does not represent the actual level of enzyme activity in the nervous system. Further carefully designed studies of occupational exposure to OPs would help to evaluate the use of this test in industrial toxicology.

In an earlier study by Lotti et al (1983) observed that S,S,S-Tributylphosphorotrithioate (DEF) and merphos are commercially used organophosphorus defoliants that are of particular interest in occupational medicine because both compounds can produce delayed neurotoxicity in animals. The putative molecular target in neural tissue for the initiation of delayed neuropathy is neurotoxic esterase (NTE). The discovery of this enzyme in peripheral lymphocytes prompted them to determine whether or not measurement of its inhibition might be useful in monitoring workers exposed to organophosphates that can cause delayed neurotoxicity. They measured the occupational exposure to DEF and merphos of seven workers during aerial and ground application of these defoliants in cotton fields by determining environmental air and dermal concentrations of the organophosphates. They also measured the NTE activity in lymphocytes before and several times during the exposure. Peripheral nerve function was measured before and after the exposure (electromyograph and nerve conduction studies) to correlate possible biochemical and physiologic effects.

AChE and BuChE remained within ± 25% of the preexposure values when measured several times during the exposure. Mean AChE and BuChE levels before exposure to DEF were 5.11 ± 1.05 umol/min/ml of blood and 2.98 ± 0.76 mmol/min/ml of plasma,

respectively. Mean lymphocyte NTE activity before exposure to DEF was 6.22 ± 3.2 nmol/min/mg of protein. NTE activity values higher than the preexposure levels were detected three times during exposure, but these values never exceeded the value determined on day 1; in both subjects lymphocyte NTE values returned to normal levels three weeks after the end of the exposure. On day 1 of exposure three of their subjects had stimulation of NTE activity in lymphocytes ranging from +40% and 80% of the preexposure values and two of them showed inhibition of lymphocyte NTE activity. However, all subjects showed inhibition of lymphocyte NTE activity ranging from -40% to 65% between days 25 and 30 of exposure to DEF. At the end of DEF and merphos exposure, all subjects were no longer exposed to any OPs; three weeks after the termination of exposure, there was a clear tendency for NTE activity in lymphocytes to return to preexposure values.

In all subjects, maximal motor conduction velocity and terminal latency in the right ulnar and peroneal nerves were normal, as were the amplitude and latency to peak of the right ulnar and sural sensory action potentials. There was no significant difference in the values obtained in the two examinations performed on each subject.

Lymphocyte NTE activity is affected in workers exposed to DEF and merphos. The initial increase in activity, which has been described in animals as well was evident in all but two of the subjects and those were probably the most intensely exposed. In all workers exposed to DEF and merphos for a prolonged period (approximately four weeks), even if exposed sporadically, lymphocyte NTE was inhibited about 40% to 60%, approaching the preexposure values three weeks after the end of exposure. This might represent a cumulative effect, considering that OPs are almost irreversible inhibitors of esterases.

If blood lymphocyte NTE activity is a good mirror of nervous tissue NTE activity, then, having observed no effect on the physiology of the peripheral nervous system in workers, it may be concluded that equally high levels of inhibition of NTE activity are required in humans as in animals to trigger the neurotoxic response. They also interpret the 40% to 60% levels of

lymphocytic NTE inhibition observed in the DEF workers as a warning that exposure had approached the toxic threshold; however, it is not known if the proximal toxin (almost certainly not DEF itself) is stable enough to reach nervous tissue and affect NTE there as much as the NTE in lymphocytes. Further animal and human studies with DEF and other potentially neurotoxic OPs are needed to establish the time and dose correlation between inhibition of lymphocytic NTE activity and neuropathologic response.

de Jager et al (1981) describe a patient with delayed polyneuropathy after suicidal ingestion of parathion. A 41-year-old farmer attempted suicide by drinking a large amount of a 25% solution of parathion in methyl alcohol. Therapeutic measures included gastric lavage, administration of atropine and obidoxime, and artificial respiration. Muscular twitching was seen, and there was excessive sweating, hypersalivation, and bronchial hypersecretion. After 7 weeks in a deep coma, he recovered, but there was flaccid paralysis of both legs and weakness of the muscles of both hands; the affected muscles were atrophic. Strength returned gradually, but 3 months later there still was marked muscle wasting and weakness of dorsiflexors and plantar flexors of the feet. Intrinsic hand muscles and proximal leg muscles were mildly weak. He walked with the aid of short leg braces. One year later he had improved, but there still was weakness of distal leg muscles; the hands were normal. Tendon reflexes were brisk, but plantar responses were flexor. He had abandoned the braces and was doing farm work.

Curtes et al (1981) describe and discuss the late neurological effects of an acute intoxication due exclusively to an organophosphorus compound, based upon a particular case they were confronted with at Rennes' Poison Control Centre. On July 11, 1972, a 21-year-old student was admitted as an emergency into a secondary hospital because of loss of consciousness and trembling. According to her sister-in-law, a psychiatrist, she presented a long psychiatric history of schizophrenia. Her mother then informed them that her daughter had drunk a bluish liquid in order to commit suicide. Later inquiries enabled them

to identify, one month later, this product as a liquid insecticide, Folimate, an alkyl thiophosphate; thiophosphate of O,O-dimenthyl and (S.N.-methyl-carbamoyl-mathyl) or Omethoate. The neurological examination showed rare myoclonus and episodes of hypertonicity. The optic fundus and electroencephalography were normal. On the 27th day a marked decrease of muscular strength was noted, also hyperactive and symmetrical tendon reflexes in the upper limbs, and symmetrical but less active reflexes in the lower limbs. On the 29th day, the patient was unable to remain upright, the reflexes were diminished with absence of Achilles tendon reflex. Electromyographic examinations performed on the 35th, 42nd, and 50th days showed total denervation at the first dorsal interosseous of the right hand, the right hypothenar region, and the tibialis anterior muscle. On the 75th day, muscle testing was normal proximally in the upper limbs, but lowered in the forearms and the wrists, and absent in the hands, while in the lower limbs power was clearly diminished in the thighs and legs and absent in the feet and in the toes. On the 100th day following her intoxication, the neuropathy began to regress. By the 9th month, the motor unit parameters showed improvement, as did the motor nerve conduction velocity (38 m/s) denervation remained practically total in the right and left tibialis anterior muscles. She was discharged from the hospital on April 14, 1973, 9 months after the intoxication. Rehabilitation continued at home. In January 1974, the 18th month, electromyography demonstrated motor unit potentials reappearing in the left tibialis anterior muscle and the motor nerve conduction velocity was normal in the upper limbs. Late neurological attacks are very rare when compared to the large number of acute intoxications by organophosphorus compounds.

## Strategies for Prevention

The widespread use of organophosphorus compounds and the associated risk of acute neurotoxicity and more remotely delayed neurotoxicity are of concern in Ontario. The most preferred

strategy to control and prevent adverse health effects would be to designate organophosphorus compounds under specific health and safety legislation for Ontario. Important aspects would include exposure reduction through engineering controls, provision of protective equipment, worker education, and biological monitoring for indices of exposure.

Further research is required to explore the neurotoxicity of other pesticides and organic chemicals and monitor for delayed manifestations of neurotoxic effects.

## CHAPTER SEVEN

## HEMATOLOGICAL DISORDERS AND FARM WORK

### Aplastic Anemia

Lorand et al (1984) observed in Brazil, a substantial increase in the incidence of bone marrow aplasia: 20 (56%) of 36 cases observed in an agricultural area near Sao Paulo related to the use of pesticides and herbicides. Some were caused by inadequate precautions when handling these chemicals.

A 42-year-old man inhaled a massive amount of 'Dipiterex', an organochlorophosphate. One week later he began to show symptoms of anaemia, fever, and weight loss, 6 months later his Hb was 5.8 g/dl, leucocytes $1.9 \times 10^9$/l ($0.4 \times 10^9$ neutrophils/l, 2% blasts), and platelets $4.0 \times 10^9$/l. Bone marrow biopsy revealed severely depressed hemopoiesis. Five months later severe CNS bleeding led to his death.

A 17-year-old female employed at a tomato plantation where several organochlorides were used presented with a 1 month history of anemia. Her sister had died 1 year earlier of bone marrow aplasia. Her Hb was 9.4 g/dl, leucocytes $1.5 \times 10^9$/l ($0.9 \times 10^9$ neutrophils/l), and the platelet count was $6.8 \times 10^9$/l. Bone marrow was moderately hypoplastic. She was treated with oxymetholone and prednisone, and her marrow function improved. One year later, only thrombocytopenia persists. She left the farm where she used to live and moved into town.

A 12-year-old girl was working in a cotton field when pesticide was sprayed from an aeroplane. One month later her Hb was 6.2 g/dl, leucocytes $3.0 \times 10^9$ ($0.3 \times 10^9$ neutrophile/l), and platelets $2.0 \times 10^9$/l. Bone marrow showed chiefly fat tissue and few hemopoietic cells. She was treated with oxymetholone and prednisone. Diabetes developed. She died 5 months later.

A 42-year-old man was exposed to an organochloride when a spray pump exploded (in an accident in which three colleagues died from acute intoxication). One month later he had a severe bleeding diathesis with gastrointestinal hemorrhage. Hb was then 5.9 g/dl, leucocytes $11.3 \times 10^9$/l (neutrophils $8.9 \times 10^9$/l), and platelets $1.2 \times 10^9$/l. Bone marrow was normocellular with an

important maturation defect, and atypical erythroblastic and granulocyte lines. Few megakaryocytes were seen. Three months later, when the bleeding diathesis had been controlled, some monocytoid cells were seen in the peripheral blood. Pancytopenia and monocytoid cells persisted peripherally for 11 months, at which time acute myelogenous leukaemia was diagnosed. He died of overwhelming infection before chemotherapy could be started.

Atanasov et al (1983) performed clinical and cytologic investigations of workers professionally exposed to pesticides. Eighty-seven workers from the Agrochemical centre of the Scientific-Production Complex (SPC) - Plovdiv intermittently working with chemical substances for plant protection have been studied, 66 of them before the start of the active work period and all of them during the period of active exposure to pesticides. Sixty-nine workers occupied with the production and composition of pesticides, with no variation in their work pattern, with an average age of 41.6 years (from 23 to 61) and an average length of service in pesticide production of 12 years have also been studied. The two groups of workers are exposed to a combined chronic effect of phosphoorganic, chlororganic, thiazine, copper and other types of pesticides. The control group consisted of 90 agricultural workers occupied in crop-producing, fruitgrowing and other agricultural activities. The clinical investigation of the workers from the two groups established a statistically proven increase of the complaints and changes on the part of the nervous system - with prevailing autonomous vascular effects, followed by changes and complaints on the part of the respiratory, cardiovascular, gastrointestinal and hepatic systems which coincides with the findings of other authors. Only skin-allergic manifestations are significantly greater in those working in production. The cholinesterase activity was supressed in 18.25% of the agricultural workers and in 8.5% off the workers engaged in production. The cytological study established a reliable reduction of Er in workers engaged in production and agriculture as against the control group. No reliable difference of Er in the agricultural workers before and in the course of active handling of pesticides was established.

Investigation of the blood picture did not show deviation with the exception of the percentage of eosinophil granulocytes eosinophil leukocytes. A statistically reliable rise in their number in the three groups compared to the control group was registered. The difference in the number of Eo between the groups studied was insignificant. No particular dependency between the changes found and the values of cholinesterase activity was observed.

Ceglowski et al (1983) reviewed the selected examples of such studies in this and other reports (3) reveals considerable diversity in terms of species of experimental animal, purity and dose of pesticide, length of exposure, and class of pesticide employed. Observations include depression, enhancement, or no significant effect on the selected reitculoendothelial system function studies. With the present available information it is difficult to formulate general conclusions or to predict whether or not any individual pesticide will consistently and significantly alter any specific function of the reticuloendothelial system. At the present time, it is not known if pesticides within a single chemical class act in a similar manner in regard to their ability to influence reticuloendothelial system function. In addition, the relationship, if any, between the toxic, mutagenic teratogenic, or carcinogenic potential of any pesticide and its ability to alter the reticuloendothelial system is also unknown. More extensive systematic studies in experimental animal models would appear to be required before protocols to effectively evaluate the potential of pesticides to influence reticuloendothelial system functions in man can be developed.

Cassimos and Panagiotidou (1983) did an epidemiologic survey of 30 children in whom idiopathic pulmonary hemosiderosis was diagnosed. Eighteen patients had died; 12 patients were still living. The majority of the cases were diagnosed in between 1962 and 1971, mainly in the spring and fall. Eighty percent of the patients lived in villages, whereas only 30% of the total population resided in the same type of rural area. Only one (5%) of the deceased children lived in the city, whereas four (33%) of the living children were city dwellers. The socioeconomic

conditions were poor, and in 50% of the cases continuous exposure to highly toxic insecticides was elicited by history and investigation of housing conditions. The incidence of newly diagnosed cases decreased with the improvement of living conditions and the prohibition of the use of certain insecticides. We believe that environmental factors, perhaps insecticides, may cause idiopathic pulmonary hemosiderosis in genetically predisposed persons. An epidemiologic history and genetic investigation should be included in the evaluation of patients with any disease when the cause is obscure.

Roberts (1983) reported that repeated exposure to commercial (technical grade) pentachlorophenol (PCP) preceded aplastic anemia in four patients and pure red cell aplasia in two. Two patients developed concomitant or subsequent Hodgkin's disease and acute leukemia. The hematologic, mutagenic, and carcinogenic effects of PCP and its chemical contaminants have been documented in other clinical and experimental reports. In view of the widespread contamination of our environment by PCP, clinicians and public health investigators must seek out such exposure in these related disorders and initiate measures to reduce it.

Wang and Grufferman (1981) did a case-control study of the association between fatal aplastic anemia and occupations entailing pesticide exposure and estimated the relative risk to be 0.67 (0.26 to 1.7, 95% confidence interval). They found no correlation between chlorinated hydrocarbon pesticide use and aplastic anemia mortality in the U.S. from 1950 through 1975 (correlation coefficient = -0.25, p = 0.28). Accumulated epidemiologic data do not support a dose-dependent causal relationship between pesticides and aplastic anemia. Alternatively, it is suggested in this study that pesticides may induce idiosyncratic reactions in rare individuals.

Morgan et al (1980) presented a recent case of severe, but reversible, hypoplastic anemia associated temporally with lindane exposure. A series of 46 cases of hematotoxicity associated with lindane is reviewed, and the weaknesses in the indictment of

lindane as the causative agent are pointed out. A more rational policy for control of agents suspected of damaging bone marrow awaits improved understanding of pathogenetic mechanisms.

Reeves and Driggers (1980) reported that Raid Ant and Roach Killer ("Raid") is a popular household insecticide containing Dichlorvos (DDVP) organic phosphate, Propoxur (Baygon) carbamate, and kerosene petroleum distillate. Three children, aged 2 to 7 years, developed aplastic anemia 4 days to 4 months after their homes were fumigated with "Raid". Two of these children initially had febrile seizures and uncompensated hemolysis and two had persistent high fetal hemoglobin concentration. One child recovered in one year and is well five years later. The second child has recurrent pancytopenia requiring corticosteroid therapy two years later. The third developed acute lymphoblastic leukemia six months after the onset of aplastic anemia and remains in continuous complete remission after 15 months of combination chemotherapy. A questionnaire subsequently completed by 309 randomly selected parents showed that 45% fumigated their households with spray insecticides during the previous two months, frequently with "Raid" type insecticides. None of their approximately 500 exposed children have apparently developed significant adverse reactions. Household use of popular organophosphate and carbamate insecticides may rarely be associated with the development of febrile seizures and blood dyscrasias in children.

Jenkyn et al (1979) have seen a patient with aplastic anemia and pseudotumor cerebri after exposure to insecticides and herbicides.

A 14-year-old girl was referred for evaluation of pancytopenia. Four months before admission she had noted easy fatigability and occipital headaches, worse on arising and associated with nausea and vomiting. Her history was unremarkable and she was not taking drugs. Physical examination was remarkable for bilateral papilloedema with flame hemorrhages. No adenopathy, organomegaly or focal neurlological signs were seen. She had been repeatedly exposed to insecticides and herbicides while working in the fields of a tobacco company

from May to October, 1976. After spraying she (and fellow workers) reported transient nausea, vomiting and malaise. She lived next to a potato farm that was also frequently sprayed, and the family had to close all doors and windows to keep out the mist. Agents to which she was exposed included zineb, zirma, malathion, carbaryl, naphthyl, and methylcarbamate. After lumbar puncture, headache and nausea decreased and the blind spots diminished to normal. The patient was evaluated for bone-marrow transplant but a compatible marrow was not found. She remained profoundly thrombocytopenic until her death from spontaneous cerebellar hemorrhage in May 1977. Necropsy confirmed intracranial, subglossal, periorbital, and intraperitoneal hemorrhage. Bone-marrow sections were unchanged. There may have been a causal association between this patient's aplastic anemia and her exposure to insecticide/herbicide preparations. The development of pseudotumor cerebri may have been a direct toxic effect of the insecticide/herbicide compounds on the absorptive mechanisms of CSF in the brain; however, it is more probably related to the severe anemia from marrow failure. Insecticide/herbicide exposure should be considered in patients presenting with aplastic anemia and/or pseudotumor cerebri.

Traczyk and Rudowski (1979) investigated organochlorine insecticides as potential factors influencing blood cell functions. Their observations of 200 subjects have revealed a significantly higher mean blood level of DDE in the group of patients with blood dyscrasias and especially with pancytopenia. The significance of this finding is not clear as yet and its mechanism is not established. The aim of their investigations was to check the influence of chlorinated insecticides on blood cells, in concentrations found in human blood. Immunological methods were applied for detection of lymphocyte sensitisation to insecticides. For revealing the antibodies the microlymphocytotoxic test was applied. They have noted a lymphocytotoxic reaction in the presence of DDT, DDE, HCH and methoxychlor in 3 out of 23 patients examined, having various blood dyscrasias and a history of exposure to insecticides. The intensity of the reaction varied. In two cases the highest degree of cytotoxicity

was noted in the presence of HCH. These results point to the presence in three of their patients of serum antibodies against DDT, DDE, and HCH - cytotoxic to lymphocytes. Their latest study concerns insecticide influence on leucocyte migration in a short-term culture with the use of microcapillary technique. The test carried out in 110 subjects revealed in about 1/4 of them a positive inhibitory effect on leucocyte migration in the presence of DDT, DDE, HCH and methoxychlor. The most frequent positive reaction was found in the group of patients with pancytopenia and plasmocytoma, this reaction significantly differed from those observed in the groups of healthy subjects and in other blood diseases. It is worth underlining that in pancytopenia, as compared with the remaining groups of blood dyscrasias, they noticed a more frequent positive inhibitory reaction to all 4 insecticides tested.

Komarova (1976) reported that the frequency of prolonged contact with pesticides was much greater among the patients with various forms of leukemia, hypoplastic anemia and hemorrhagic diathesis than among the patients with nonhemorrhagic diseases. Cytochemical changes were found in the leukocytes of practically healty persons engaged in the production and use of chlororganic pesticides. The amount of DDT and of its main metabolite DDE proved to be greater in the hemopoietic organs of persons who died of hypoplastic anemia than in their subcutaneous cellular tissue - the main depot of the pesticides accumulating in the organism. An unfavourable influence of the prolonged DDT action on the course of leukemic process was confirmed in experiments on animals.

Palva et al (1975) presented a 64-year-old farmer who developed aplastic anemia after exposure to 2-methyl-4-chlorphenoxyacetic acid while spraying weed killer. Muscular weakness, hemorrhagic gastritis and slight signs of liver damage occurred at the same time. All these symptoms, including blood dyscrasia, are consistent with those described as toxic effects of chlorphenoxyacetic acids in animal experiments. A causal relationship between aplastic anemia and the 2-methyl-4-chlorphenoxyacetic acid thus seems probable. The anemia was

reversible, but the case serves as a warning that careful safety measures are required during the use of chlorphenoxyacetic acids and related compounds.

Holmes et al (1974) reported two cases of acute, moderate toxicity to mevinphos. Symptomatology was similar to that previously reported for exposure to parathion or sarin. Excretion pattern for the alkyl phosphate ester dimethylphosphate (DMP) shows rapid excretion that is almost complete 50 hours after exposure to mevinphos. Total excretion of DMP equivalent to 7.7 mg and 9.2 mg, respectively, of mevinphos was measured in two cases. Blood coagulation studies showed marked fibrinolysis in one case and marked hypercoagulability in the other, as demonstrated by the thrombin generation curve. Hematuria persisted in one patient for more than eight days. Both patients responded well to treatment. There was a five to ten-hour delay between exposure and the patient reporting to the hospital for treatment.

Embry et al (1972) looked for altered urinary excretion of heme precursors and catecholamines in workers occupationally exposed to pesticides and have evaluated chemical exposure and absorption by (1) measurement of serum chlorinated hydrocarbon contents, (1) determination of blood cholinesterase activities, (3) urinary excretion of the parathion metabolite paranitrophenol, and (4) protocols of the chemicals with which participants have been in contact.

Samuels and Milby (1971) presented the results of a clinical and laboratory appraisal of a group of human subjects who were exposed to lindane for periods of several weeks to several years. Particular emphasis was placed on methods for detecting the presence or absence of significant hematopoietic depression, in an effort to determine, if possible, whether aplastic anemia or other detectable hematopoietic disorders result from exposure to lindane under the conditions of this study. The study population consisted of 79 individuals, all of whom had been exposed to lindane on almost a daily basis for periods varying from a few

weeks to many years. The study population was divided into five groups on the basis of intensity of exposure to lindane as judged by observation of work practices and multiple air sampling for lindane.

Immune Disturbances

Dean and Padarthsingh (1981) discuss practical applications of immunology to toxicology, environmental health, and regulatory programs. Topics are discussed under the following headings: the biology of immune suppression and regulation (intrinsic and extrinsic regulation of immune responses, immunopharmacology of immunotherapy, heterogeneous interaction of cytotoxic immunodepressants with immunocyte subpopulations), measurements of immunologic parameters (measurement and assessment of immune competency, effects of anti-cancer and their application to prognosis, investigation of the immunobiological effects of polybrominated biphenyls in Michigan farmers, and the potential of high resolution protein mapping as a method of monitoring the human immune system), experimental changes in immunologic parameters following exposure to environmental agents (immunological alterations in mice following acute adult exposure to diethylstilbestrol, effects of environmental chemicals on host defense responses of the lung.

Kurisaki et al (1979) studied the effects of paraquat on human embryonic somatic cells. Monolayer cultured cells, from several different organs, were exposed to various concentrations of paraquat. Then the cells were stained with nigrosine and Sudan IV to demonstrate dead or damaged cells and fatty granules, respectively. The lowest paraquat concentration that caused morphological changes varied from 1 to 10 ppm; and the lowest concentration that caused fatty degeneration varied from 1 to 5 ppm. In both types of staining, the lowest degenerative concentration was lower as the culture generation was younger, and the degree of degeneration did not differ with the cell origin. The protein content per cell in paraquat-treated cells was not significantly decreased in comparison with control cells.

Bekesi et al (1979) examined 11 Michigan chemical workers and 46 non-exposed Wisconsin farmers. Abnormalities included decreased number of T-lymphocytes with concomitant increase of lymphocytes with no detectable surface markers, "null cells", and altered lymphocyte function. Data obtained from skin testing using standard recall antigens, showed no consistent correlation between the delayed cutaneous hypersensitivity response and the impaired lymphocyte function. PBB (hexa) in separated white blood cells and red cells was positively identified and quantified by gas chromatography-mass spectrometry. PBB and immunological abnormalities were not detected in non-exposed Wisconsin dairy farm residents.

Takahashi et al (1976) determined gamma mobility C-reactive protein (CRP) level was determined in the sera of persons occupationally exposed to pesticides and controls in conjunction with serum protein analysis and other biochemical and enzymologic tests. Workers chronically exposed to dieldrin and pentachlorophenol showed significantly higher prevalence of CRP than the unexposed persons. In addition, the pentachlorophenol-exposed subjects revealed significantly elevated levels of total bilirubin and creatine phosphokinase, although the levels were within normal limits. The results suggest that chronic exposure to pentachlorophenol may have been responsible for the difference in the prevalence of CRP between the pentachlorophenol and control groups.

Ercegovich (1978) reviewed the subject of pesticide-immunological interactions. Conflicting views exist about the extent of hypersensitivity caused by pesticides. Sensitization to high doses of pesticides, as evidenced by dermatitis, may be more prevalent than previously supposed. However, there is no documented information which reveals that exposure to low dosages of pesticides in the form of residues in foods are overtly responsible for hypersensitivity. Production of antisera responsive to protein conjugates of parathion and amitrole, and to metabolites of DDT and malathion has been achieved by several

groups. A limited number of experiments have demonstrated varying effects of abnormal doses of pesticides on immunologically controlled defense mechanisms in laboratory animals and on the synthesis of -globulin, but no evidence has been presented thus far which reveals that incidental exposure to pesticides elicits these effects in humans.

Ceglowski et al (1979) on reviewing the effects of pesticides on the reticuloendothelial system observed that the information available concerning the effects of compounds utilized as pesticides on functions of the reticuloendothelial system is quite limited. Review of selected examples of such studies in this and other reports reveals considerable diversity in terms of species of experimental animal, purity and dose of pesticide, length of exposure, and class of pesticide employed. Observations include depression, enhancement, or no significant effect on the selected reticuloendothelial system function studies. With the present available information it is difficult to formulate general conclusions or to predict whether or not any individual pesticide will consistently and significantly alter any specific function of the reticuloendothelial system. At the present time, it is not known if pesticides within a single chemical class act in a similar manner in regard to their ability to influence reticuloendothelial system function. In addition, the relationship, if any, between the toxic, mutagenic, teratogenic, or carcinogenic potential of any pesticide and its ability to alter the reticuloendothelial system is also unknown. More extensive systematic studies in experimental animal models would appear to be required before protocols to effectively evaluate the potential of pesticides to influence reticuloendothelial system functions in man can be developed.

# CHAPTER EIGHT

## PESTICIDE EFFECTS ON OTHER ORGAN SYSTEMS

### Organophosphates

Brill et al (1984) observed that organophosphate insecticide intoxication produces endogenous acetylcholine poisoning which may precipitate complex ventricular arrhythmias, a relatively unrecognized and potentially lethal aspect of this condition. A case is described in which sinus bradycardia, A-V dissociation, idioventricular rhythms, multiform ventricular extrasystoles, and prolongation of the PR, QRS, and QT intervals were observed. Polymorphic ventricular tachycardia - a chaotic ventricular rhythm characterized by extreme variability of QRS morphology and the R-R interval - which previously has not been reported with organophosphate poisoning, was also present in our case. Metabolic and electrolyte derangements, myocardial injury, autonomic dysfunction, and asynchronous repolarization variously may be involved in the genesis of arrhythmias in organophosphate intoxication. Management of these cases should take into account the possible occurrence of conduction abnormalities and arrhythmias,including polymorphic ventricular tachycardia.

Wren et al (1981) reported a case of complete heart block following exposure to an organophosphate insecticide. Implantation of a permanent pacemaker was followed by repeated problems with exit block. A 52-year-old dairy farmer was first seen in 1974 complaining of breathlessness, aching legs and weakness after using an organophosphate insecticide (Ruerene). Physical examination and ECG were normal and avoidance of the chemical led to a complete recovery. Re-exposure in 1975 produced a recurrence of his symptoms and thereafter he avoided the chemical completely. Eight weeks before admission in 1979 he accidentally touched an opened can of Ruerene (4 tert-butyl-2-chlorophenyl methyl methylphoramidate) and three days later he had his first blackout. In the following few weeks he had many similar attacks, several of which were witnessed by his family and were typical Adams-Stokes attacks. He also complained of

anorexia, abdominal cramps, profound weakness and severe dyspnoea on exertion. There was no history of angina and he had been quite well in the past. He was a non-smoker.

Albright et al (1983) report a case of acute renal insufficiency with massive proteinuria after exposure to the organophosphate malathion. A 65-year-old man was admitted to the hospital because of swelling of his legs. Four weeks before admission, he began spraying intensively with malathion and noted intermittent inhalation and skin exposure. Three weeks before admission, he noted an increase in weight and, subsequently, peripheral edema. He had a five-year history of diabetes mellitus treated with insulin. He intermittently took cimetidine for dyspepsia. He denied use of nonsteroidal anti-inflammatory agents. This patient experienced acute renal insufficiency with massive proteinuria that rapidly resolved without any specific treatment. The presence of membranous glomerulopathy and a marginally reduced C3 level suggests antigenic exposure with subsequent immune complex deposition in the kidney. The development of overt renal insufficiency with massive proteinuria within three weeks of exposure to malathion suggests a causal relationship. Although the patient had no symptoms attributable to organophosphate poisoning, he may have had a latent exposure without clinical manifestations, although cholinesterase activity may be inhibited. Organophosphate exposure might cause immune complex formation by one of two mechanisms. Antibodies might react with the organophosphate directly or to native antigens that have been unmasked by a direct toxic effect of the organophosphate. It is postulated that malathion provoked an immune complex nephropathy in this patient resulting in renal insufficiency and massive proteinuria, and the authors stress that this toxic agent must be handled accordingly.

Dagli and Shaikh (1983) did a prospective study to find the incidence of pancreatic involvement in malathion poisoning. Cases admitted to the medical unit of a general hospital with a definite history of malathion ingestion were taken up for the study. In all 75 cases were studied. History and physical

examination were done of each case. None had any significant past illness and were not taking any drugs. They were investigated to find the incidence of pancreatic involvement. Of the 75 patients included in the study, 47 were women and 28 were men. The majority of the patients (67 out of 75) were in the age group of 16 to 30 years. All the patients had consumed malathion in a liquid form. In the absence of past history of abdominal illness and or recent history of drug ingestion and since the pancreatitis has been reported in organophosphorus insecticide poisoning, it is believed that the pancreatic involvement which occurred in 47 patients in the study was due to malathion-organophosphorus insecticide intoxication. Since the raised amylase value in all 47 patients returned to normal within 3 days, the authors felt that the occurrence of both the acute pancreatitis (10 patients) and slight pancreatic involvement (37 patients) must be mild and transient.

Dwzarzy et al (1982) reported the results of acetylcholinesterase and cholinesterase activities in erythrocytes of subjects occupationally exposed to the phosphoorganic pesticides compared to the control group. Simultaneously glycaemia was assessed with the aid of 3-point sugar curve. In the studied group statistically significant decrease in the activity of both esterases and abnormal sugar levels both after night fast and following oral glucose load were found. Moreover, detected increase in glycaemia in subjects exposed to phosphoorganic pesticides show negative linear correlation with the degree of AchE and ChE inhibition. The authors suggest possible hyperglycaemic activity of the phosphoorganic compounds (not detected in man as yet) in subjects chronically exposed to such compounds.

Dressel et al (1979) observed that severe pancreatitis and a pseudocyst occurred in a patient following accidental ingestion of an anticholinesterase insecticide, a substance not previously known to produce pancreatitis. Experiments were done to elucidate the mechanism. In one group of dogs the pancreatic duct was perfused and intraductal pressures were measured. In a second group of dogs pancreatic secretory rates were measured.

In a third group of dogs administration of cholinesterase inhibitor 75 mg/kg and secretin infusion 2 U/kg/hr resulted in acute pancreatic interstitial edema, acinar cell vacuolization, hyperamylasemia and hyperlipasemia. The results suggest that occurrence of pancreatitis as a complication of anticholinesterase insecticide intoxication is the result of hypersecretion and pharmacologic ductal obstruction.

Sobti et al (1982) studied the cytotoxic, cytostatic, and cytogenetic effects of 14 organophosphate pesticides on human lymphoid cells in vitro. The compounds tested were azodrin, diazinon, dichlofenthion, dimethoate, dursban, ethion, fenthion, malathion, methyl parathion, parathion, phorate, phosdrin, R-1303, and viozene. Cultures of human lymphoid LAZ-007 cells were exposed to the test compounds at concentrations of 0.02, 0.2, 2.0, or 20 ug/ml for 48 hours with or without metabolic activation by rat-liver microsomal S9 product. The frequency of sister chromatid exchanges (SCE) was significantly increased by 11/14 organophosphates, S9-actiavation increased the rate of SCE only with diazinon, dimethoate, and phosdrin.

## Carbamates

Koizumi et al (1979) presented the case of a 62-year-old man who spread maneb on about 200 sq m of garden and subsequently was taken to the emergency clinic with complaints of oliguria, diarrhea, and hoarseness. Based on the clinicobiochemical data, he was found to have acute renal failure; the serum levels of BUN, creatinine, and potassium were 144.3 mg/dL, 14 mg/dL, and 5.8 mEq/L, respectively. The STL segment depression in $V_{4-6}$, reciprocal ST segment elevation in $V_{1-3}$, and inverted T waves in $V_5$ and $V_6$ were recorded on ECGs. Both the renal failure and the ECG abnormalities disappeared after hemodialysis. The possibility exists that the maneb caused the acute renal failure.

## Phenoxyacetic Acids

Torrington (1983) reported an unusual exposure which took place in 1982 to Karmex. It is a common practice in the railroad industry to reduce the foliage along the tracks by spraying herbicides such as 2,4-D or Karmex. During the spring of 1982, two healthy young men, an engineer and conductor, received an intense exposure to these herbicides. The train was being driven into a strong head wind while pushing tank cars containing the herbicides in front of the locomotive. Significant amounts of the spray were whipped by the wind into the locomotive as it pushed the spraying unit along. The herbicide spray opacified the front windshield of the locomotive, making it constantly necessary for the engineer and conductor to lean out of the side windows in order to drive the train. After the second day of the spray both patients noted symptoms of itching and burning involving their oral and nasal mucosa and their conjunctiva. In areas where their skin had sweated or had made contact with glasses frames, small ulcerations appeared. Within 24 hours both men developed significant chest discomfort with cough, which was initially productive of a mucoid sputum. They complained of mild headache, some muscle twitching, and throat soreness. Within the next 4-5 days, the cough and sputum production decreased, but both patients continued to feel somewhat weak and dyspneic. Both are concerned about the possibility of long-term pulmonary toxicity. The exposure of these men to 2,4-D and Karmex may have been more intense than exposures previously reported Factors such as the duration of exposure, particle size of the aerosol, and biological properties of the vehicle may have been of importance.

Paraquat

Levin et al (1979) described the clinical and pathological features of a patient who died from the effects of percutaneous absorption of paraquat. The toxin was absorbed during the spraying of vineyards. Nine of his co-workers, less heavily exposed, were investigated. The transfer factor for carbon monoxide was reduced in six. Lung biopsy of two showed medial

hypertrophy of the pulmonary arteries with evidence of fresh and organised thrombi. In one there was also interstitial fibrosis. They designed an experimental animal model to investigate these findings. Low concentrations of paraquat were applied to the skin of rats over a nine-week period. The lungs were examined postmortem, and the medial thickness of the muscular pulmonary arteries was expressed as a percentage of their external diameters. In randomly encountered (large and small) pulmonary arteries the mean percentage medial thickness (MT%) was 11.99 $\pm$ 0.41% (SEM) in controls and 25.28 $\pm$ 0.94% in test rats ($P < 0.001$). In the large muscular pulmonary arteries the MT% in the control rats was 13.6 $\pm$ 0.49% and in the test rats 25.9 $\pm$ 1.44% ($P < 0.001$). In the small pulmonary arteries the values were: controls 9.0 $\pm$ 0.73% and tests 14.2 $\pm$ 1.35% ($P < 0.05$). One test rat which died spontaneously showed pulmonary infarction from thrombosis. They concluded that paraquat absorbed through the skin in low dosage over a prolonged period can produce pulmonary arterial lesions in man and rat. This contrasts with the familiar pathological findings of acute high dose ingestion. These findings have important bearings on the use of this herbicide in agriculture.

Mullick et al (1981) reported 13 patients who developed evidence of hepatic damage after exposure to paraquat and subsequently died. At autopsy, the main changes involved the bile excretory pathways. Ten of the 13 cases had cholestasis, usually localized to the centrilobular zone. There was cholangiocellular injury involving the small and medium-sized bile ducts in portal areas. It consisted of shrinkage of cells, poor definition of outline, separation from the basement membrane, desquamation of cells into the lumen, infiltration of the wall by neutrophils and possible loss of integrity of the basement membrane. These bile duct lesions have not been previously described in association with paraquat toxicity. On the basis of the overall histologic findings in this study and extrapolation from experimental studies, it is hypothesized that paraquat injury to the liver is biphasic; it is initially hepatocellular but becomes cholangiocellular after the first 2

days.

Vaziri et al (1979) performed renal function studies in three cases of paraquat poisoning. Acute renal failure was observed in all three cases. Glomerular filtration rate improved for two patients who survived three weeks, illustrating the reversible nature of paraquat-induced acute renal failure. A mild to moderate transient proteinuria was observed during the first and second weeks following paraquat ingestion. Renal glucosuria, marked amino aciduria, and increased fractional excretion of phosphorus, sodium, and uric acid were observed. These findings, which have not been previously described in man, are indicative of proximal tubular dysfunction and parallel observations previously made in experimental animals.

## Others

Villar (1974) commented on the use of "Bordeaux mixture" to prevent the development of mildew on grape vines and described the pathologic changes produced in the lung by inhalation of this pesticide. Fifteen cases of vineyard sprayer's lung were analyzed in an attempt to define the various clinicopathologic forms of the disease and methods of diagnosis. The remarkable incidence of lung cancer in these patients is stressed.

Pimental and Marques (1969) observed that the mildew of the vineyards is prevented by the use of sprays with a solution of copper sulphate neutralized with hydrated lime. The inhalation of this solution while spraying may give rise to predominantly interstitial pulmonary lesions which may lead to respiratory insufficiency. These lesions, which were experimentally reproduced in guinea-pigs, have a well-defined histological picture characterized by three stages - intra-alveolar desquamation of macrohages, formation of predominantly histiocytic granulomas in the septa, and the healing of these lesions generaly under the form of fibro-hyaline nodules very similar to those found in silicosis. These lesions contain variable amounts of copper. The pathogenesis of these lesions

and the possibility of their regression when the offending agent is removed are discussed; and the value of lung biopsy and the necessity of protecting these workers are stressed.

# CHAPTER NINE

## SKIN DISORDERS AND FARM WORK

Peachey (1981) reviewed skin hazards in farming. In the course of his occupation, the average farmer engages in a wide variety of activities including the rearing and feeding of animals, milking, veterinary care, treatment of soil and crops, harvesting and the maintenance of the farm buildings and machinery. Although workers on the farm are thus exposed to many possiible skin hazards, no survey has been carried out in Britain to assess the incidence of skin problems in this group and little information is available for other countries.

He reviews the main categories of dermatological hazards to farmers, particularly those in the United Kingdom. It is not meant in any way to be comprehensive and concentrates particularly on those hazards which have become more common with the increasing sophistication of farming techniques.

VanJoost et al (1984) reported that contact dermatitis occurred in a man, aged 40, who worked for about 2 years in a chemical factory. In this factory, a variety of chemicals are used in the manufacture of products which are used for the control of pests.

The raw materials used are 3-chlor-4-fluoraniline (CFA) and mesylchloride (MSC). The following solvents and additicves are used: NaOH, triethylamine (TEAM), toluene, methylisobutylketone (MIBK) and SBP 65/70 (special boiling point, hydrocarbon mixture boiling in the rante (65-70 $^{o}$C). In the production mesylisopropyllactate (MIPL) is an important intermediate product. The patient developed an eczematous eruption on both hands and on the left upper leg in September 1982. After his work was discontinued and the skin lesions were treated the eczema disappeared within 3 weeks. On resuming his work as a process operator, a similar eruption reappeared on the arms (not on the hands), the face and hips after a short period.

Moses et al (1984) reported that chloracne was found in 52% of 226 workers in a 1979 cross-sectional survey at a plant where

2,4,5-trichlorophenoxyacetic acid (2,4,5-T) had been manufactured from 1948 to 1969. Mean duration of residual chloracne was 26 years, and in 29 subjects, it had been present for 30 years. A significant increased prevalence of abnormal gamma-glutamyl transpeptidase (GGT) and higher mean GGT were found in those with chloracne, compared to those without. Although mean triglyceride values were higher in those with chloracne, the difference was not statistically significant. Neurological examination showed a statistically significant higher prevalence of abnormal sensory findings in those with chloracne. Increased prevalence of angina and reported myocardial infarction in those with chloracne was not significant when age-adjusted. Increased prevalence of reported sexual dysfunction and decreased libido in those with chloracne compared to those without was statistically significant after age adjustment. No differences were found between those with and without chloracne in serum cholesterol, total urinary porphyrins, or in reproductive outcome.

Brown (1984) describes 2 further cases of Captafol sensitivity from the same laboratory. The first, a 37-year-old male research chemist who, after several years away from contact with Captafol, once again became interested in research on certain aspects. He had, in his first period of work with the substance, noticed towards the end that occasional contact resulted in skin irritation and a mild rash on the hands with irritation of the periorbital and nasal skin. Prick testing confirmed his atopic status. There was no evidence of contact urticaria from open tests on the forearms.

The second case is that of a female graduate chemist aged 26 years who had worked in the laboratory for 6 months, mixing pesticides for biological evaluation. For 2 months she was engaged in mixing Captafol and another chemical without any problem. After alternative work, she returned to mixing the same 2 chemicals, and next day developed a blotchy rash on the neck and cheeks which cleared with oral antihistamine treatment and avoidance of the chemicals. Her hands were unaffected despite not wearing gloves. Skin contamination had been minimal. Sensitisation had nonetheless developed. This is in keeping with

the view that Captafol is a potent sensitiser.

Garcia-Perez et al (1984) compared the results obtained with a standard patch test series in a group of agricultural workers with a control group. Statistically significant differences in the frequency of several allergens were found. The possible causes of these differences are discussed.

Van Joost et al (1983) reported 3 new cases of sensitivity to benomyl (Benlate, methyl-1-butylcarbamoyl-2-benzimidazole carbamate) in combination with simultaneous sensitization to other pesticides in 2 patients. The patients were tested with benomyl 1% in petroleum ether. After testing with this concentration, no skin reactions were seen in 10 control persons by van Ketel, who reported benomyl sensitization in a man growing mainly begonias.

Toby Mathias (1983) reported that a driver of a truck transporting a commercial formulation of the insecticide, dichlorvos, developed unusually persistent contact dermatitis following accidental skin contact, as well as systemic signs of organophosphate toxicity. The mechanism was presumed to be irritant rather than allergic.

Austad and Kavli (1983) reported that 11 men developed a severe phototoxic dermatitis of the hands and forearms after harvesting celery infected with Selerotinia selerotiorum. By thin-layer chromatography and fluorescence spectrophotometry, xanthotoxin, bergapten and sphondin were isolated. The Candida albicans test demonstrated Xanthotoxin and Bergapten as the phototoxic compounds.

Nishioka et al (1983) observed that a man, with a dermatitis acquired while working in a factory producing a weed killer, showed sensitivity to 4-methylsulfonyl 2,6-dinitro-N,N-dipropylaniline (DNA-nitralin) and its precursor, 4-chloro 3,-5-dinitrophenylmethyl sulfone (DNC), and cross-sensitivity to dinitrochlorobenzene (DNCB). Sensitization capacities of DNA-nitralin and DNC compared with DNCB, and cross-sensitizations among 11 dinit-

robenzene derivatives, including DNA-nitralin, DNC, and DNCB, were studied in guinea pigs. It was found that the order of potency was DNCB, DNC, and DNA-nitralin for the sensitization capacity, and that cross-sensitizations might occur among DNCB, DNC, DNA-nitralin, and dinitrofluorobenzene, in comparatively high incidence.

Pasricha and Gupta (1983) report a case of contact dermatitis due to calcium ammonium nitrate used as a fertilizer.

Malten (1983) reported on a patient who worked on her husband's chicory farm. She had an allergic contact dermatitis for the past 3 years on her hands, arms, face and V of the neck from September to April. Her trouble began 6 months after the chicory farm was established. Eating the leaves as vegetables caused a stomatitis. She reacted on patch testing to the root and Witlof leaf.

Tucker and Flannigan (1983) determined through a field survey, the prevalence of cutaneous response to the synthetic pyrethroid fenvalerate; to characterize the cutaneous reaction; and to identify the setting in which it occurs. The methodology involved case studies of selected individuals who had worked extensively with fenvalerate in the delta region of Mississippi and Alabama. All the agricultural workers interviewed and examined had, on some occasion, noted a parasthesia which they associated with exposure to this pyrethroid insecticide. The cutaneous sensation described was a stinging or burning which progressed to numbness in approximately one-third of the exposed workers. The sensation typically began a number of hours after contact, peaked in the evening, and rarely was present the following morning. The intensity of the sensation varied according to the type and extent of exposure. Clinical signs of inflammation such as edema or vesiculation were not apparent. Erythema was present in a limited number of individuals but was not distinguishable from sunburn. Several environmental factors were found to affect the cutaneous sensation associated with fenvalerate exposure.

Johnsson et al (1983) reported on tetrachloroisophthalonitrile (TCPN), an agricultural and horticultural fungicide used in many parts of the world. In Northern Europe it is also used as a wood preservative. The substance has well-known toxic properties through skin contact, and has recently been reported as inducing allergic contact dermatitis. They report an epidemic of contact dermatitis in a Norwegian wooden-ware factory, which they attribute to TCPN. Fourteen out of 20 workers had skin complaints which were work related. Half of these cases were shown to be of allergic origin. The toxic and allergic properties of TCPN render this compound unsuitable for use in the wooden-ware industry. A reevaluation of its use in agriculture and horticulture seems appropriate.

Reuveni and Yagupsky (1982) saw ten soldiers because of an eruption in the antecubital fossae. All of them had used an insect repellent containing 50% diethyltoluamide a few hours before the eruption had appeared. The symptoms and clinical findings in these cases were those of a burning sensation, erythema, and blisters at the onset, followed in some cases by ulceration and scarring. Precautions in the use of this commonly used repellent should be advised.

Adams and Manchester (1982) reported on a case of a 15-year-old supermarket clerk who experienced a severe, widespread, blistering dermatitis, chiefly on her arms, trunk and face. The eruption recurred repeatedly and at times was explosive at onset, especially on windy days. Treatment with topical corticosteroid preparations and oral triamcinolone provided only temporary relief.

Patch testing with a standard battery of test materials was negative except for a strong positive reaction to thiuram. A test battery of agricultural chemicals was then applied, because of the patient's belief that the dermatitis was caused by an "insecticide" of some sort. Patch testing revealed a strong reaction to Maneb, 1% in pet. There was no reaction to Zineb.

Because the patient's husband was a home gardener, she submitted a list of the pesticides used in his work. Among 14

different products, a lawn fungicide "FORE" was found to contain manganese ethylene bisdithiocarbamate, or Maneb. On questioning the husband, we learned he had stored a large bag of this substance, a loose powder, in their garage near the washer and dryer. After removing the fungicide and thoroughly cleaning the garage, the patient's dermatitis rapidly disappeared and has not recurred during the 15 months since.

Viein et al (1980) reported on nine farmers suspected of having occupational contact dermatitis who had positive patch tests to spiramycin and/or tylosin. After diagnosis the dermatitis cleared or improved markedly in seven patients; five of these stopped using the antibiotics in question, and two began to wear gloves while handling the drugs. The two patients who continued use of the drugs and took no precautionary measures had little change in the activity of the dermatitis.

Withers et al (1979) documented a painful deep second degree burn of the scrotum and perineum in a nurseryman exposed to paraquat concentrate. A 40-year-old white male nurseryman presented to Vanderbilt University Hospital one week following exposure to paraquat. While using a shoulder supported spray cannister his pants became soaked with paraquat solution, and eight hours later he noted an intense burning pain in his thigh, scrotum, and perineal area. He consulted a physician who initiated topical steroid therapy. One week later, due to progression of his symptoms, he was seen in the plastic surgery clinic, where physical examination revealed a deep second degree burn of his scrotum and healing first and second degree burns of his thigh and perineum. Chest x-ray, BUN and creatinine were normal. A 100-ml urine sample tested for paraquat was negative.

Boren and Leky (1979) began a retrospective study to investigate dermatitis in duck workers. Seventeen cases were certified. The charts were reviewed for appearance of lesions, predisposing factors, laboratory tests, culture results, and final disposition. The duck farm was inspected by both a physician (SDB) and a veterinarian (BJL).

Zachariae (1978) commented that ethoxyquin is an antioxidant which has been used for many years in pig feed. Ethoxyquin has previously been known to cause contact dermatitis in apple packers from ethoxyquin used with a detergent to prevent apple scald. Last year he found three patients with contact to pig feed in which ethoxyquin may have been the causative agent of a contact dermatitis.

Calnan (1982) reported that a woman aged 28, has had eczema since early childhood and hay fever for ten years. She has a family history of eczema and hay fever. Over the past year, she noticed that contact with several vegetables caused itching. Examination showed moderately extensive atopic eczema with lesions on the hands. The Cornish greens handled by this patient usually refer to young cabbages.

Caplan (1973) reported that drug additives can also provoke uritacarial reactions and diffuse dermatitis, via the airborne route in farmers and feed-mill workers. Furthermore, farmers often engage in do-it-yourself veterinary care for their animals and, thus, have contact exposures to solutions of penicillin and other drugs.

Hearn and Keir (1971) reported on nail damage in spray operators exposed to paraquat. Nail damage in 55 persons due to contamination by diluted paraquat in a group of 296 spray operators employed on a sugar estate in Trinidad is described. The commonest lesions seen was transverse white bands of discoloration, but loss of nail surface, transverse ridging, gross deformity of the nail plate and loss of nails occurred. The index, middle, and ring fingers of the right hand were predominantly affected and this could be ascribed to leakage from the knapsack sprayer. It is emphasized that, although the degree of contamination was unusually gross, it is nonetheless important to recognize that the diluted material can cause nail damage. Simple hygienic precautions and proper maintenance of spraying equipment can prevent its occurrence. Periodic medical examinations are recommended even for workers exposed only to

diluted paraquat. The distribution of the nail lesions confirms that they are the result of a local action. Following cessation of further exposure subsequent nail growth is normal.

Verspyck Mijnssen (1969) investigated the pathogenesis of the occupational skin disorder known as "tulip finger" showed it to be determined by an allergic mechanism. Paper-chromatography of active extracts from tulip bulbs, and subsequent patch-tests with these paper-chromatograms in sensitized individuals, made it possible to localize the allergic principle in the paper-chromatrograms and to find a reagent for chemical spot tests with the active agent. In later experiments the Tollens reaction was used to locate the active substance in paper-chromatograms, without doing patch tests. Qualitative analysis indicated a compound related to sugars, which is probably a glucoside. Hydrolysis of this compound yielded glucose, and a substance identified by chemical, spectroscopic and gas-chromatographic methods as: x-methylene-y-butyrolactone.

# CHAPTER TEN

## MONITORING OF PESTICIDE EXPOSURE

### Introduction

In this chapter, various methods of monitoring of pesticides are reviewed. Specific types of pesticides are covered highlighting routes of exposure, mode of absorption, measurement of biological specimens, and possible control measures.

Franklin et al (1982) observed that the assessment of potential health hazards to workers resulting from the use of pesticides requires a knowledge of both the amount of pesticide to which a worker is exposed and its toxicity. There are numerous variables which may affect the actual levels of pesticide in the workplace. One way to minimize their effect on the estimate of exposure would be to group the variables into subgroups or scenarios which describe a set of operational circumstances common to a specific use. If field studies are conducted in which the variables are clearly delineated, it is possible that a model could be developed that would predict the maximum exposure under registered use conditions, and such a model would be of great value in the assessment of hazard to workers. This approach may be feasible for the orchard scenario because of the large number of studies that have been carried out. Some of the factors which should be taken into consideration in developing an exposure model and areas where there are insufficient data to make an accurate estimate were discussed.

### Organophosphates

Franklin (1984) reported on estimation of dermal exposure to pesticides and its use in risk assessment. The potential risks to humans resulting from the usage of a pesticide must be carefully assessed before the product is registered. One of the components in the risk assessment is the determination of the

amount of pesticide to which the applicator is exposed. Traditional methods estimated dermal exposure by measuring the amount of pesticide deposited on absorbent patches worn on the applicator's body. A more recent approach consists of measuring urinary metabolite levels. A review of data obtained in humans and in rats suggests that the urinary concentration of dimethyl thiophosphate is a good indicator of dermal exposure to azinphosmethyl.

Coye et al (1984) reviewed patterns of intra- and inter-individual variation in cholinesterase activity, the effects of disease, genetic variation and other factors, laboratory and field methods for biological monitoring of cholinesterase activity among populations occupationally exposed to organophosphates, epidemiological surveys of cholinesterase activity among agricultural workers, and the correlation between cholinesterase activity and symptoms of acute and chronic illness. They discuss the biologic monitoring of exposed workers for intact pesticides and their metabolites. They summarized current biological monitoring practices and presented some thoughts on potential developments in biological surveillance programs for agricultural workers.

Lerman et al (1984) describe the potential use of a computerized medical information system that includes clinical data on 236 cases of OP and carbamate poisoning, and may improve the management of such poisoning. The methods of constructing the system, the first results of using the system, and the medical institutions that can benefit from such systems are discussed.

Rhyanen et al (1984) investigated the fact that garden workers may have a high pesticide exposure and an increased incidence of occupational related health problems. Unfortunately only a limited amount of data is available on the actual chemical loading of the garden workers. Blood cholinesterase activities can serve as useful indicators in organophosphate pesticide exposures. The measurement of erythrocyte acetycholinesterase and plasma cholinesterase at the same time is favorable, because

these enzymes may be inhibited to different degrees and for differing time periods after an exposure to organophosphates. However, the collection and storage of blood samples for activity measurements is a problem under field conditions. The separation of erythrocytes and plasma before transport is time-consuming and centrifugation is needed. The unknown amount of hemolysis during preparation and transport is a potential disadvantage when whole blood samples are used. The reactivation process of the phosphorylated or carbamoylated cholinesterases is one considerable source of error. A technique of applying samples of whole blood on filter paper has earlier been reported and applied under tropical conditions to avoid these difficulties. The aim of the present study was to test the suitability of this method with slight modifications in the follow-up of occupational exposure of garden workers.

Davis et al (1983) investigated potential exposure of apple thinners to azinphosmethyl and comparison of two methods for assessment of hand exposure. To establish the time that must be allowed to elapse before workers can safely re-enter a crop that has been sprayed with pesticide, one must be able to estimate the hazard associated with working in the crop at any particular time after application of the pesticide.

Kraus et al (1981) describes the results of a long-term monitoring study of 36 grape harvesters who were occupationally exposed to organophosphate pesticide residues following reentry into vineyards during September and October 1976. The study was designed to evaluate the biochemical parameters associated with organophosphate pesticide exposure, to relate the occurrence of changes in these parameters to environmental residues of cholinesterase-inhibiting pesticides, and to evaluate techniques for monitoring the health of agricultural workers routinely exposed to organophosphate pesticide residues.

Kraus et al (1981) evaluated biological parameters associated with organophosphate (OP) pesticide exposure in a study of citrus harvesters. Changes in these parameters related to environmental residues of cholinesterase (ChE) inhibiting

pesticides were studied. Further, it was determined whether usual and nonusual workers differed in their biochemical parameters after exposure to pesticide residues during field operations. Urine metabolite findings for usual farm workers showed that some exposure to OP pesticides had occurred. Too few workers were available during the reentry stage of the field study to evaluate the effect of this exposure on blood ChE. Baseline (nonexposure) acetylcholinesterase (AChE) and plasma cholinesterase (PChE) activities were significantly higher in usual (Mexican American) workers than in non-usual workers (student volunteers). Student volunteers in the test citrus grove showed statistically significant declines in PChE during the exosure period, yet changes in AChE activity, urine metabolites, and residue levels were very small. The implications of these findings are discussed in light of current reentry standards as well as future epidemiologic studies on reentry research.

Davies et al (1982) reported that systemic pesticide illness in agricultural workers may result from excessive dermal exposure to pesticides. Workers who apply and mix pesticides (applicators and mixers) are at special risk. Both acute and chronic exposures can occur from spillage or by environmental contamination of clothing. Two exposure assessment studies were conducted of Central Florida citrus grove workers who applied ethion daily. Measuring the percentage of penetration of ethion through clothing and measuring the daily urinary excretion of diethyl phosphate (DEP) were the techniques used to assess the protection afforded by changing daily to freshly laundered 100% cotton coveralls. Coveralls provided significantly greater protection than did regular clothing and the use of respirators.

Davis et al (1982) undertook a study to determine the potential dermal and respiratory exposures that experienced apple thinners received while working in orchards shortly after the Federal reentry interval for phosalone (s((6-chloro-2-oxo-3-benzooxazolinyl)methyl)0,0-diethyl phosphorodithioate).

Franklin et al (1981) estimated exposure to and absorption of Guthion 50 W.P. (azinphos-methyl) in orchardists from the Okanagan Valley in British Columbia who were involved in mixing, loading, and application with ultra-low volume air blast equipment. Air monitoring and patch techniques were used to estimate exposure, and alkyl phosphate excretion and cholinesterase inhibition were measured to estimate absorption. All workers were issued with standardized cotton shirts, trousers, and long-sleeved coveralls. All wore half-face respirators, gloves, boots, and hats. Eight wore rubberized protective clothing in addition. The indirect method of measuring urinary metabolites appeared to be the most sensitive. All workers had quantifiable levels of alkyl phosphates following exposure, and the 24-h urine samples provided a more reliable estimate than first morning voids. A high correlation was observed between 48-h alkyl phosphate excretion and amount of active ingredients sprayed. A fluorescent tracer was added to the tank along with the Guthion. The finding of Guthion on patches beneath the clothing was confirmed by the presence of the tracer on the skin. With the ultralow-volume application used in this study, the rubberized clothing did not appear to be significantly more protective than the heavy coverall. There was no significant depression of either red blood cell or serum cholinesterase activity in any workers.

Nigg (1980) reported on worker safety reentry research and identified needs for future development in this area.

Popendorf et al (1979) undertook a field study to quantify the exposures of peach pickers to pesticide residues. Five fields were harvested each for three days at decreasing post-application intervals. Aerosol and dermal exposure estimates indicated 98-99% of the workers' dose was dermal, predominantly to the hands and upper extremities. Estimates of dose correlated with measurements of foliar residues. Despite estimated dose rates of up to 14 mg/hr, the RBC cholinesterase in these workers may have been only slightly inhibited (circa 4%) when compared to an unexposed, control population. Comparisons of these results with earlier studies of parathion residues on citrus

indicate a consistent pattern of worker exposure. However, a concern is raised over the efficacy of using existing foliar residue sampling methodologies for all other pesticides.

Young et al (1979) investigated phorate intoxication at an insecticide formulating plant. On February 13, 1971, a 34-year-old black male employed by a formulation plant was admitted to a hospital around noon. He was unconscious and his employer reported that he was suffering from organic phosphate insecticide poisoning. The following symptoms were noted during his treatment period: confusion, dizziness, nausea, vomiting, and constricted pupils.

On May 21, 1971 an 18-year-old black male employed at the same formulating plant was brought to a hospital emergency room in severe respiratory distress. He was exhibiting the following symptoms: cardiac arrhythmia, excessive salivation, respiratory distress, muscle fasciculation, and pinpoint pupils.

In the worker's breathing zone, phorate concentrations ranged from 0.07 to 14.60 $mg/m^3$.

In the formulating plant described in this paper, personal protective equipment was used to supplement inadequate ventilation controls in the mixing and bagging of phorate.

All samples taken during the formulating operation exceeded 10 times what eventually was adoped as the TLV. One sample was almost 300 times this value. From the worker's description of conditions, dust levels must have been even higher for the second poisoning incident. It is of utmost importance that a respirator program include the elements of proper selection of respirators, individual fitting, worker training in respirator use, and maintenance of the units. However, even with a good program there will probably be some exposures close to 10 percent of the ambient concentration.

Meier et al (1979) identified a toxic impurity, 0,0,0,0-tetraethyl dithiopyrophosphate (sulfotepp), in pesticide formulations of diazinon. Organophosphorus pesticides such as diazinon are widely used because of their acute toxicity to insect pests and short persistence after application.

They have been studying methods for the chemical degradation and disposal of pesticide wastes. Studies with four different diazinon formulations demonstrated that acid hydrolysis significantly reduced the diazinon concentration, however, there was less than 50% reduction in the toxicity of the reaction mixture to aquatic organisms.

Wicker et al (1979) monitored plasma and red blood cell cholinesterase levels of professional agricultural workers engaged in packing sweet corn and thinning peaches. Workers with extensive contact with mechanically harvested sweet corn (the corn had been treated one or two days before harvest with a combination of ethyl and methyl parathion) exhibited significant depression of cholinesterase. Gloves, worn by 40% of the workers, provided some protection from absorption of pesticide residues. No significant cholinesterase depression was found in workers thinning peaches which had been previously treated with parathion.

Richards et al (1978) measured blood acetylcholinesterase (ACHE) and pseudocholinesterase activity and urinary dialkyl phosphate excretion in a group of 15 male agriculture field workers during a five-day thinning operation in a Northern California peach orchard. Eight men randomly assigned to work in a Guthion-treated plot, and seven men to work in an adjoining plot free from organophosphate residues. Foliage samples were taken to measure dislodgeable and total Guthion residues. The daily mean percent change in the ACHE and in the PCHE activity was less than - 10.0 percent of baseline values for each group of men. Mean ACHE activity of workers in the Guthion treated plot was different from that of workers in the control plot on the fifth exposure day. The mean PCHE activity of workers in the Guthion treated plot was not different from that of workers in the control plot. Daily group-mean urinary metabolite excretion levels for workers exposed to Guthion residues were highly correlated with their daily group-mean percent change in ACHE activity. No urinary metabolites were detected in workers in the control plot. Decay in Guthion residues was markedly slower in this trial than in a comparable study conducted one year

previously, emphasizing the difficulty in setting re-entry intervals based on time elapsed from pesticide application. Suggestions were made to extend the time interval of future studies on the human health effects of organophosphate residue exposure, and to refine urinary metabolite surveillance methods toward the goal of establishing a threshold level of metabolites which would correspond to meaningful exposure to these pesticide residues.

MacKintosh et al (1978) studied the apparent increase in the number of people in Rhodesia suffering from the effects of organophosphate poisoning. The writers decided to study a few aspects of the problem as a field project in Community Medicine.

Fournier and Sonnier (1978) describe techniques for determining human exposure to organophosphate insecticides by gas chromatography.

Bach et al (1978) assessed a diagnostic dip-stick for measuring pseudocholinesterase activity and compared it with a standard spectrophotometric method. Duplicate dip-stick estimations (measured in kU/l) corresponded closely, and concurrence between participants was good. The dip-stick estimate of cholinesterase was consistently lower than the spectrophotometric value; the magnitude of this deviation depended on the absolute enzyme activity. With enzyme activities of up to kU/l the dip-stick value was 1 unit lower. Between 1 and 4 kU/l the dip-stick estimate compared well with the spectrophotometric value. From 5 to 7 kU/l and beyond 7 kU/l the negative deviation recorded by the dip-stick increased to 2 units or more.

Normal enzyme activity is 3-6 kU/l. Over the 1 - 4 kU/l range the method is most accurate, thus negative deviation below 1 kU/l or above 4 kU/l is generally diagnostically irrelevant. On the basis of cost, convenience, speed and accuracy this method will suffice in the absence of sophisticated assay facilities.

Lores et al (1978) reported the analyses of four organophosphorus pesticide poisoning cases, three of which

resulted in death. The case histories of the subjects, along with the analysis of tissues, urine, and blood for the levels of pesticides and metabolites are given. The pesticide involved include dicrotophos, chlorpyrifos, malathion, and parathion. The methods of analysis were adapted from previously published methods that provide a very rapid means of identification of organophosphorus pesticides in the tissues or in the blood of poisoned patients.

Knaak et al (1978) obtained blood samples from workers through cooperating physicians in farm worker health clinics during the growing and harvest season for lettuce, grapes, peaches, and citrus in January, May, July, and September, 1975. The blood samples were analyzed for cholinesterase activity. The mean plasma (8.3) and red cell (27.9) cholinesterase activities of female field workers were not significantly different from those of nonfield workers or field workers who had not worked in the field during the last 30 days. The mean red cell cholinesterase activity (27.7) of male field workers was significantly lower than the red cell activity (29.6) of nonfield workers in 1975 but not different from field workers who had not worked during the last 30 days (27.5) or nonfield workers in 1976 (27.5). The mean plasma cholinesterase activity of male field workers (9.9) was not significantly different from those of nonfield workers (9.4) in 1975 or 1976, whereas field workers who had not worked in the field during the last 30 days had plasma values (8.9) significantly lower than those working. Red cell values of field workers returning for a repeat test were found to increase slightly between the first test and second, although plasma values remained the same.

Serat (1978) commented on existing methods for the calculation of worker entry intervals by the use of kinetic data focusing on the anticholinesteratic organic phosphates. As carbamate pesticides share with these materials a common site for inhibition, the kinetic method was applied in estimating an entry interval for the carbamate, carbofuran, applied to citrus and grapes as Furadan 4F. No allowance was made for the more transient carbamylation of cholinesterase attributed to N-methyl

carbamates, compared with the phosphorylation of the enzyme by organic phosphates. Thus, a measure of safety was built into the calculations which can then be used to establish safe reentry intervals to insure residue levels below the physiological threshold for cholinesterase inhibition.

Smith (1977) investigated organophosphorus poisoning from emergency use of a handsprayer. In the Midlands, in 1976, wheat was infested by aphids to an unprecedented extent. Tractors destroy about 10% of the standing wheat; aerial spraying can be done in large fields but is impracticable for small areas or adjacent to crops such as fruit that are ready for harvesting. In view of the suddenness of the infestation, neither light plane nor helicopter spraying services were able to take on all the emergency work and farmers urgently sought other means of aphid control.

Spear et al (1977) reported on the residue intoxication hazard of parathion. The investigations were carried out in June and July 1974 with the object of determining the route of exposure of orange harvesters to parathion residues, identifying the important toxic constituents of the foliar residue and determining the residue levels at which biochemical responses would occur. Preliminary investigations had suggested that the principal route of exposure was dermal and that, in the organge groves of the Central Valley of California, paraoxon was the prinicpal intoxicant.

Robbins et al (1977) describe monitoring observations made on a crew of orchard workers in a large, well-managed, central Washington orchard to determine if measurable or observable effects could be detected which were attributable to their normal occupational exposure. A crew of orchard workers originally consisting of thirty persons, twenty-four of whom listed agriculture as their usual or principal occupation and six of whom were local residents employed for the summer only, was selected on a volunteer basis and the planned monitoring program was explained to them in detail. Blood samples for

cholinesterase were collected by standard venipuncture techniques and urines were collected for analysis for alkyl phosphate metabolites. If values of cholinesterase for those workers who indicated that their principal occupation is agriculture are separated from the "summer only" employees, plasma cholinesterase levels are significantly higher at the 5% level for the agricultural workers than for the "summer only" employees. Values of red blood cell cholinesterase were also higher, but did not reach significance at the 5% level.

Talcott et al (1977) correlated the titer of malathion carboxylesterase in liver and sera of rats, three strains of mice, and five groups of pretreated mice with the malathion LD50 values measured in these groups. The equation of a regression line relating enzyme titer to toxicity was used to predict the median lethal dosage of purified malathion to humans. The mean value, 3655 mg/kg, was compared with dosages ingested in actual cases of human malathion poisonings. A discrepancy was noted between the LD50 value predicted in this study and the life-threatening doses of commercial malathion reported in the clinical literature. The unexpectedly high toxicity of commercial malathion may be related to its content of esterase-inactivating impurities.

Comer et al (1976) determined cholinesterase enzyme activity of a blood sample from a child poisoned by parathion. The child was to be in the hospital several days for observation following treatment, so it was decided to obtain blood and urine samples from the child once a day for six days. They used these samples to correlate cholinesterase values with the concentration of o,o-diethylphosphorothionate (DETP), o,o-diethylphosphate (DEP) and para-nitrophenol (PNP) in urine and to study the stability of these metabolites in refrigerated urine samples.

Kashyap and Gupta (1976) evaluated toxicological effects of ultra-low volume (ULV) aerial spray of phosphomidon, a highly toxic organophosphorous insecticide, in 38 human volunteers. Results of medical surveillance and serial estimation of pre- and post-exposure blood cholinesterase enzyme activity in red cell

and plasma are reported. A single ULV aerial application of phosphomidon in doses of 550 g/hectare produces irritation of eyes and conjunctivae in the majority of cases, at the time of insecticidal application. No other clinical manifestations were noticed. Observations on blood plasma ChE activity showed a significant depression in 75 per cent volunteers. This was noticed on the third day of application and the activity gradually recovered by the ninth day. The inhibition of red cell cholinesterase activity was not significant.

Kuo and Fong (1976) determined P-nitrophenol in urine and it has been proved that urinary p-nitrophenol is a better index of exposure to parathion than blood cholinesterase activity. But the recovery reported by Elliott was 73% only, and furthermore it needs 100 ml of urine for a determination. In order to obtain a higher recovery, the Mallinckrodt method was used with slight modification. This gave a 93.7% recovery and the sensitivity was also about 25% higher than that of Elliott's method. In two parathion formulating factories, some workers and clerks were subjected to urine analysis by this method, and the results showed that urinary p-nitrophenol in workers could be detected even after expoure to parathion for only one day.

Rider et al (1975) used four groups, of five human volunteers each, they were fed various doses of mevinphos daily for 30-day periods to determine its effect on plasma and erythrocyte (RBC) cholinesterase with the following results: 1.0 mg had no effect, 1.5 and 2.0 mg each produced a 20% or greater decrease in RBC cholinesterase on one occasion only, while 2.5 mg produced a steady decrease in RBC cholinesterase reaching a maximum of 25% on the 27th day of administration. None of these doses affected the plasma cholinesterase activity. From these results it was concluded that 2.5 mg mevinphos meets the criterion for minimal incipient toxicity, which is defined as the amount producing a decrease of 20-25% below control cholinesterase activity.

Wolfe et al (1975) performed studies of potential exposure

of a volunteer working under controlled conditions during apple hand-thinning operations. At 1, 24, 48, 72, 96, 168, and 240 hr after application of conventional 0.03% parathion spray, both dermal and respiratory exposure values were greater where water-wettable powder formulations were used than where emulsifiables were used. Residue levels of parathion on leaves from the two types of applications were about the same. Only trace amounts of paraoxon could be detected at one and seven days after application. Highest exposures values (14.2 mg/hr dermally and 0.15 mg/hr respiratorily) were obtained within 24 hr of application. Exposure was considerably less after residues were 72 hr old. Greatest exposure was on the forearms and hands. Urinary p-nitrophenol excretion indicated slightly more absorption following exposure in water-wettable powder experimental plots. Potential exposure values indicate that absorption could reach hazardous levels after one or two hr of work, even at the 96-hr residue period, if all the pesticide were absorbed. Considering that only a small fraction of the total amount would be absorbed, it is calculated that at 72-hr residue period poisoning should not occur. There was no significant change in blood cholinesterase activity of the volunteer worker. Variation in spray deposit within an orchard due to poor tank mixing did not appear to be great enough to be considered an important factor affecting exposure.

Wolfe et al (1975) investigated potential exposure of workers to parathion through contamination of cigarettes. Potential hazard from smoking pesticide-contaminated cigarettes has not been clearly defined. Research on amount of residues of organophosphorus pesticides present in tobacco or tobacco smoke as a result of application to the growing crop has been carried out. However, the authors know of no published work related to potential exposure of spraymen or other workers from smoking cigarettes that have become contaminated with a toxic organophosphorus compound through handling by workers in the field or from pesticide drift during application. When gloves are not worn the hands often become the most heavily contaminated body parts during pesticide application operations. This is probably at least partly due to the fact that they frequently

come in direct contact with the more concentrated forms of pesticides during mixing and loading. The practice of smoking without washing hands, or smoking during pesticide application operations where there is potential for drift of pesticide onto an opened package of cigarettes carried in a shirt or coverall pocket, raises the question of the contribution of such contamination to the worker's total daily exposure.

Carbamates

Gold et al (1982) monitored 38 urban volunteers from the Lincoln and Omaha, Nebraska areas for carbaryl exposure during the summer of 1979. All volunteers were involved in the application of carbaryl incidental to their employment or leisure activities. The investigators made no attempt to affect the method of carbaryl application. The mean rates of carbaryl exposure were 3.85 and 0.26 gu $cm^2$ $hr^{-1}$, respectively, for the outside of the clothing and the skin beneath the clothing; clothing apparently provided an effective barrier to carbaryl penetration. The rate of carbaryl exposure to the hands of applicators was 2.36 and 24.96 ug $cm^{-1}$ $hr^{-1}$, respectively, for applictors with and without gloves. The maximum dermal exposure recorded in this study was 2.86 mg $kg^{-1}$ $hr^{-1}$ which is significantly less than the estimated dermal $LD_{50}$ value for carbaryl (4000 mg $kg^{-1}$). The maximum air concentration of carbaryl was 0.28 ug $L^{-1}$, far less than the Threshold Limit Value of 5 ug $L^{-1}$. Only a small mean decrease was found in the applicators' serum (-1.01%) or erythrocyte (-1.39%) acetylcholinesterase activity. Although some applicators had decreases in either serum or erythrocyte acetylcholinesterase activity greater than 20%, an equal number had increases of the same magnitude. The mean total carbaryl exposure to the applicators, expressed as a percent of toxic dose per hour, was 0.01%, with a maximum estimated exposure of 0.08%.

Comer et al (1975) investigated exposure of workers to carbaryl. Since the carbamate pesticide, carbaryl (1-Naphthyl N-methylcarbamate), was first registered for agricultural use in

1958 it has enjoyed a reputation as one of the safest compounds as far as hazard to man is concerned. Using the combined mean dermal and respiratory potential exposure values obtained in the present study of formulating plant workers and spraymen, the calculated percent of toxic dose per hour of exposure would be only 0.03% for formulating plant workers and 0.02% for spraymen. Even the highest exposure value obtained represents only 0.4% of a toxic dose per hour of work. These exceptionally low calculated values, of course, reflect a wide margin of safety to workers exposed to carbaryl considering the relatively low toxicity of the compound. At these dosage levels concern about acute toxic effects in workers would be minimal; however, in this study the interest is in the fact that quantity-wise the body is subjected to relatively high levels of the compound. When no great additional effort is involved in providing protection from excess exposure over that which is normally practised when working with more toxic pesticide compounds, it seems wise to put forth that effort even when working with a compound of low acute toxicity. As much of the skin area as possible should be covered with protective clothing in order to avoid excess absorption of the compound, whether spraying in the field or working in the formulating plant. Where exposure is to dry formulations of carbaryl the respiratory route takes on increased significance and warrants the use of tight-fitting cartridge-type respirators, especially when working at the mixing or bagging stations in the formulating plant.

## Phenoxyacetic Acids

Franklin et al (1982) observed that although the technology of spray application has shown remarkable progress during the past decade, relatively little information is available about the field exposure of workers to phenoxy herbicides. Most of the scientific data submitted to support the product registrations now on the market were developed many years ago.

Factors generally recognized to affect worker exposure are: 1) the climatological (synoptic) or micro-meteorological conditions at the time of spray operation; 2) the formulation or

mixing of spray chemicals; 3) the maintenance and adjustment of the spray equipment; 4) the maneuverability of the aircraft; 5) the flying skill of the pilot; 6) the attitude of crew members in handling the chemical; 7) the use of protective clothing; 8) the time and period of exposure; and 9) the surface geometry of the field and the growth stage of the crop.

The uptake of sprayed herbicide by the body of a person exposed directly or indirectly to the spray, and its subsequent fate in the body, are determined by the following factors: 1) the dissemination of the spray; 2) the transport of sprayed material in the atmosphere; 3) its inhalation, deposition on the skin, or ingestion and subsequent absorption; 4) metabolic transformation and/or transport; and 5) excretion. At the present time, only a limited amount of scientific information is available on the dissemination and absorption and excretion of herbicides.(6)

The objectives of this study were to determine the amounts of herbicide inhaled, deposited on, absorbed and excreted by spray applicators in routine operations in relation to various relevant factors, and to use the results obtained to suggest guidelines for estimating and controlling the occupational exposure of spray applicators to phenoxy herbicides.

Libich et al (1984) measured occupational exposures to herbicides among 12 applicators in 1979 and 24 applicators in 1980, who were applying the three herbicides, 2,4-D, dichloroprop and picloram to electric power transmission rights of ways. In 1979 only urine was analyzed but in 1980 both breathing-zone air samples and urine were analyzed for herbicide residues. Dermal absorption was found to be the major absorption, route being up to 50 times greater than exposure by the inhalation route when using a hand gun sprayer. Even with the mist blower herbicide application method, dermal absorptioon was 4 and 11 times greater than exposure by the inhalation route. Worker education on hazards of skin contact and improved protective equipment significantly reduced the 1980 urine concentrations of herbicide residues. A model is presented to relate the urinary concentrations to equivalent daily exposure levels.

Williams (1982) reviewed the literature on pentachlorophenol (PCP) and its salts (primarily the sodium salt), are thought to be among the most versatile pesticides now in use in the United States. In fact, collectively they are the second most heavily used pesticides in that country. The versatility of PCP is due in large part to its solubility in both organic solvents and water. The greatest amount of PCP is used in the wood preservative industry.

Coutselinis (1977) commented on the toxicity of 2,4-dichlorophenoxyacetic acid (2,4,5-T), widely used as herbicides in domestic and agricultural situations and provided further information on the concentration levels of these compounds in viscera in cases of fatal, accidentally or suicidal, poisonings.

## Captan

McJilton et al (1983) report the results of an evaluation of exposure to apple orchard sprayers during the application of captan. The methodology is based on the sampling protocol developed by Homer Wolfe. Dermal exposure was determined by analyzing cellulose pads which had been attached to shoulders, back and chest. Respiratory exposure was evaluated by using a modified single cartridge respirator. This method was originally developed by Wolfe to eliminate contamination of the sample by oversize, non-respirable droplets. The dermal and respirator pads were extracted with a hexane-acetone mixture and analyzed by gas chromatography.

Stevens and Davis (1981) undertook a study of the potential for exposure to captan of workers involved with various aspects of potato planting. Estimates were made for potential dermal and respiratory exposures. These exposures were termed potential rather than actual because no estimates were made for dermal absorption or for the fractions of the material collected on respirator pads which would be of the correct size to be retained in the lungs.

Hansen et al (1978) determined residue levels of azinphosmethyl and captan from blotter paper patches attached to the clothing of personnel participating in an orchard spray program. Average exposure of 1.74 mg/man/hr for azinphosmethyl and 1.94 mg/man/hr for captan were extrapolated from mean residue values obtained from analyzing the patches. Azinphosmethyl residue found on apple and peach foliage had been reduced by 69% by the tenth day post-application, while captan residue had been reduced 50% for the same period. There was no evidence of a buildup of either azinphosmethyl or captan on treated foliage as the season progressed.

## Paraquat

Lings (1982) saw a fruit-grower with large, atypical lung infiltrations and lung fibrosis. This triggered off an investigation of fruit-growers during the spraying season. An interview was carried out together with a Wright peak flow meter test and an x-ray examination of the chest. No fewer than 156 spray preparations were used by the group; individual fruit-growers used between three and 27. In connection with spraying, 41% of subjects had one or other type of symptom; peak flow was reduced in 19% and x-ray changes were seen in 24%. A questionnaire was returned by 132 of 235 farmers. Of these, 60 had worked with biocides, 72 had not. A non-significant higher frequency of symptoms was found among those who used biocides. The results would indicate that biocides (or "pesticides") can give rise to a lung disease, "biocide lung," which comprises (1) pneumonia, radiologically demonstrable by more or less transient round infiltrations and (2) chronic progressive lung fibrosis.

Howard (1980) reviewed the likely worker exposure to paraquat in agricultural practice, using correct procedures, with particular reference to the possibilities of oral, dermal and inhalational absorption. The available evidence indicates that at recommended dilution rates systemic effects do not occur.

Local effects on skin and mucous membranes may occur as the result of the delayed caustic effects of this herbicide, but experience has shown that paraquat is unlikely to give rise to serious problems when properly used.

Knepsil (1979) comments on the need for rapid and reliable estimation of plasma-paraquat concentrations. The radioimmunoassay involves several steps, including the use of an activated charcoal suspension to remove unbound radioactive paraquat, and the whole method requires skill and complex equipment which may not always are readily available in an emergency. The colorimetric method referred to is much simpler than the radioimmunoassay but emulsification can be a problem unless the extraction is done very gently over a long period. A colorimetric method has been described which involves no more than the addition of two simple reagents with short, vigorous mixing, a short centrifugation step, and addition of a single colour-developing reagent before measurement of paraquat. The sensitivity of the method is comparable with that of the colorimetric procedure referred to above, and a single analysis takes less than 20 minutes.

Proudfoot et al (1979) measured plasma-paraquat concentrations in 79 patients who had ingested liquid or granular weedkillers containing paraquat. At any given time after ingestion, the plasma-paraquat concentrations in the patients who died usually exceeded those in the survivors. It is suggested that measurement of plasma-paraquat concentrations is useful in assessing the severity and predicting the outcome of poisoning. Patients whose plasma concentrations do not exceed 2.0, 0.6, 0.3, 0.16, and 0.1 mg/l at 4, 6, 10, 16, and 24 h respectively are likely to survive.

Howard (1978) reviewed dermal exposure to paraquat. The fatal percutaneous absorption of paraquat underlines the importance of observing the label instructions in all handling of pesticides. Skin contamination is a risk in field operations with any pesticide, especially in countries where heat and humidity preclude the extensive use of protective clothing. Paraquat,

being caustic, has local irritant effects, but it is poorly absorbed through intact skin, particularly at spray strengths, and it has had a very good safety record in agriculture since it was introduced in the early 1960s.

The local effects underline the need for careful handling of this herbicide, particularly in the concentrated form, and for attention to personal hygiene. Such advice would be given for any irritant or caustic material, and even where sensible precautions are neglected local lesions usually heal with no permanent after-effects. The experience gained over 15 years in worldwide use would suggest that paraquat is most unlikely to give rise to serious health problems under normal conditions of use, even when handled for many years.

Fitzgerald et al (1978) investigated paraquat poisoning in agricultural workers. Between 1968 and 1977 thirteen male agricultural workers were admitted to hospital because of symptoms which followed the agricultural use of paraquat (Gramoxone). The results of their enquiries into the records of the Poisons Information Centre confirm that there are frequent problems with the agricultural use of paraquat in Ireland. This high level of reporting of agricultural accidents may be the cause of the belief that serious illness and fatality may result from the normal use of paraquat or may be the result of this awareness. This study fails to incriminate paraquat as a cause of serious poisoning in circumstances where it is used with due care and proper equipment. The instructions on the Gramoxone labels are not now complete in their coverage of possible dangers, and it is suggested that these are amended as follows:

1. Inclusion of instructions to the operator to ensure that the spraying apparatus is free of blockages and leaks.

2. A statement which highlights the danger of putting any part of the spraying apparatus in contact with the mouth.

3. A statement that workers who are suffering from skin disease should avoid usage altogether.

Finally, the label should more vividly state that paraquat is a dangerous substance, must be handled with extreme care, and the instructions followed to the letter.

A detailed investigation of 13 cases of poisoning, which occurred following agricultural use of paraquat is presented. Six patients died. The degree of poisoning was trivial or mild in the remaining seven. Carelessness by the spray operator led to poisoning in the majority of cases. Five cases had attempted to clear blockages in the spraying apprartus by sucking or blowing the outlet of the spraying lance. It is suggested that the warnings to spray-operators on the labels of paraquat containers should be extended to cover all of the dangers in usage.

Staiff et al (1975) reported exposure to the herbicide, paraquat. The herbicide paraquat was used extensively during of grasses and certain weeds. It is available to farmers primarily as paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride) 29.1% liquid concentrate containing 239.6 grams paraquat cation per liter (2 lbs paraquat cation per gal). The paper reports results of studies designed to determine the potential exposure of workers in the field operating conventional low-pressure power spray equipment and persons applying paraquat in yard and garden areas using pressurized dispensers. Potential hazard to small children who may handle the pressurized dispensers was also investigated. Results of the above studies on dermal and respiratory exposure to paraquat indicate that hazard to both field applicators and persons using the yard and garden pressurized dispenser is minimal when used under the conditions described. The inability to detect paraquat in the urine during and following exposure in this study indicated that absorption of the herbicide was minimal. However, these findings should not detract from the need to be concerned about ingestion of even small amounts of the concentrated formulations. The storage of the herbicide in soft drink bottles, or any container that is not the original properly-labeled container, presents one of the greatest hazards, especially to small children who may accidentally drink the material.

## Organohalides

Angerer et al (1983) studied metabolism of -hexachlorocyclohexane (HCH) examining 21 workers producing this insecticide. Using gas chromatography in combination with ECD and mass spectrometry 14 mono-, di-, tri- and tetrachlorophenols were identified in the urine samples of the workers. Seven dihydroxychlorobenzenes of still unknown configuration were detected by mass spectrometry. Ten of the more abundant metabolites, di-, tri and 2,4,6-; 2,3,5- and 2,4,5-trichlorophenol turned out to be the main metabolites of -HCH. They were excreted in nearly equal quantities. On account of their potential liver toxicity, the determination of chlorophenols in urine should be part of a biological monitoring program of HCH-exposed persons.

Putnam et al (1983) monitored ten pesticide applicators in Michigan, Wisconsin, and Minnesota for dermal and inhalation exposure to nitrofen (2,4-dichlorophenyl p-nitrophenyl ether) during typical mixing and spraying operations on onion, carrot, cabbage, and celery crops. The variables studied were formulation (emulsifiable concentrate (EC) vs. wettable powder (WP)), handling (open vs. liquid pumping), body location (palm, leg, arm, chest, head), and protective garments (best protection vs. minimal protection scenarios). Handling the WP formulation provided the highest potential dermal and inhalation exposure, much of which occurred during the mixing operation. Nitrofen deposits on the hands, a major site of dermal exposure, could be reduced by an average factor of approximately 220 by using rubber gloves. Potential daily exposure was reduced more than half by using the EC rather than the WP formulation, even if no protective garments were worn. Total exposure was reduced approximately 78% by pumping vs. pouring the EC formulation and more than 90% by handling pumped EC compared to WP. Daily exposure can be reduced to less than 300 when wearing a protective coverall plus an air filtration system and when handling the EC formulation.

Wolff et al (1979) performed clinical and laboratory examinations on 55 industrial workers and 28 dairy farmers exposed to PBB. PBB was detected in the sera of all 55 workers at levels of 1.1-1,729 ppb and in the adipose tissue of 27 workers at levels of 0.50-581 ppb. The highest serum and adipose tissue levels of PBB were found in the 10 individuals who had worked in PBB production from 1970-1974. The fat/serum PBB ratio was 287. Serum and adipose tissue PBB and PBB homolog levels were higher among the chemical workers than among the farmers.

Kraul and Karlog (1976) during the years 1972-73 obtained samples of human abdominal fat, as well as brain and liver tissue from 82 subjects, and analysed for persistent organochlorinated compounds. Compared with the figures from a similar 8 years old Danish study, no downward trend in the content of DDT and its metabolites in the fat tissue was found, while the residue of dieldrin nearly halved during the period. Polychlorinated biphenyls (PCB) were found in a mean concentration of 3.8 mg/kg fat tissue.

Kazen et al (1974) analyzed hexane hand rinsings by electron capture and flame photometric gas-liquid chromatography for pesticide residues to determine whether these chemicals persisted on the skin long after exposure. Chlordane and dieldrin have apparently persisted on the hands of a former pest control operator for at least two years. Methoxychlor, captan, and malathion persisted for at least seven days on the hands of a fruit and vegetable grower. Parathion was found on the hands of one man two months after his last known contact with it. Endosulfan, DDD, kelthan, dacthal, trithion, imidan, and guthion may have persisted on the hands of some exposed workers from 1 to 112 days after exposure.

Summary

The opportunity to design and evaluate preventive stategies to reduce the health problems associated with pesticides in Ontario should be viewed as one of urgency. Unfortunately the health care system that now delivers occupational health services is not organized in such a way to meet the needs of agricultural workers.

The National Coalition Against the Misuse of Pesticides in a report on the Federal Government and the incidence of pesticide poisonings: conducted a survey of migrant and rural health clinics and found the following:

1) The Environmental Protection Agency and the Bureau of Community Health Services are not communicating with clinics about services that are available to aid them in the detection and treatment of pesticide poisonings. Approximately 70% of the clinics were not aware of the training programs for clinic personnel, the Pesticide Incident Monitoring Service and the toll-free telephone number to aid physicians in the field. About 78% of clinic personnel had not received any training the the last year.

2) Of the 4028 total poisonings reported in this survey, only 23 were reported to PIMS.

3) Only two clinics reported having their own pesticide poisoning detection equipment; only 38% reported having local access to such equipment.

4) Of the 48 clinics that reported any poisonings, 47% indicated that among their patients with suspected poisonings, very few or none were aware of the cause of their illness.

Salter and Leiss (1984) in their final report on Consultation in the Assessment and Registration of Pesticides made the following recommendations:

1) Agriculture Canada should establish an Information Secretariat whose mandate would be the collection and

dissemination of information about pesticides to the general public, to members of advocate, labour and environmentalist groups, to members of grower and other interest groups, to manufacturers of pesticides and their representatives, to other participating Federal Departments, and to all Provincial authorities charged with responsibility for regulating pesticides.

2) Agriculture Canada, through the Information Secretariat, would produce and disseminate a 4-5 page information sheet on the chemicals being assessed for registration or re-evaluation. These backgrounders would be produced to promote informed participation from advocate, labour or environmentalist groups, grower and other interest groups, manufacturers, and Governmental authorities.

3) Decisions released by Agriculture Canada on registrations, changes in labels or re-evaluations would be accompanied by a detailed rationale and would be made available to the public by publication in the <u>Canada Gazette</u> and through a mailing list to all interest groups and individuals.

4) Agriculture Canada, through its Information Secretariat, would operate a service for callers with requests for information, complaints, or concerns about pesticides.

5) The Minister of Agriculture should establish a Pest Management Advisory Board to make recommendations on broad policy questions and on issues of special concern.
Immediately upon their appointment, the Pest Management Advisory Board should conduct an inquiry into and make recommendations on the following policy questions and other policy matters related to the registration of pesticides.

- a program for the re-evaluation of pesticides in use;
- registration procedures for pesticides for minor crop use;
- the advisability of temporary and emergency registration and the conditions, if any, under which the current practices of Agriculture Canada with respect to temporary registration should be expanded.

- methods to be used in assessment and the advisability of using a risk-benefit approach;
- ways in which the registration process could be made more efficient without detracting from the soundness of the assessments being done;
- ways in which regional needs and problems and the needs of special populations at risk can be taken into account;
- any changes in the registration process or the legislation governing registration;
- response to demands for intra-Canadian or international harmonization of regulations and standards.

6) Acting on recommendations from the Minister, from the staff of the Pesticides Division of Agriculture Canada, the Information Secretariat or members of the public and groups concerned with the assessment and registration of pesticides, the Pest Management Advisory Board should advise the Minister on the mandate for and appointments to consultative committees. These consultative committees would serve on an ad hoc basis and would consider issues requiring a special assessment.

7) A number of initiatives should be taken to support the Provincial role in pesticide regulation. One member of the Information Secretariat would have special responsibility for liaison with Provincial authorities on a day-by-day basis. Provincial authorities would then be consulted routinely when decisions were being taken on registration or re-evaluation. Regional needs could be identified, as could measures necessary to protect special populations at risk.

These recommendations, if acted upon, would begin to address major issues in the prevention of pesticide related illness in Canada.

# CHAPTER ELEVEN

## PULMONARY DISEASES AND FARM WORK

### Introduction

Farm workers' lung diseases were reviewed by Seaton (1984). A breathless farm worker may present a diagnostic challenge to the doctor. The doctor consulted by a farm worker who has become short of breath should bear in mind the three most common occupational causes. Occupational asthma is usually recognised by the patient as being associated with peculiar activities; commonly it starts shortly after he enters a barn or byre. It may occur in up to 15% of farm workers and is often associated with rhinitis or lachrymation. Farmers' lung, which may be seen in up to 5% of farm workers, typically presents as an acute attack of fever, malaise, and breathlessness four to six hours after handling mouldy stored hay. Silo fillers' lung occurs after exposure to oxides of nitrogen from the top of an unventilated silo. Cases occur sporadically owing to carelessness or lack of education of farm workers. The gas is not particularly irritant, so that the initial exposure may hardly be noticed, but cough and breathlessness increase over several hours, eventually progressing to frank pulmonary edema.

Cockcroft and Dosman (1981) reviewed respiratory health risks in farmers, who may be at risk of developing several respiratory health disorders as a result of inhalation of substances suspended in their environment. Despite the large number of farmers in Canada and the United States, information on their respiratory health status remains limited and epidemiologic studies relating respiratory symptomes to lung function in farmers have just begun. Recent work has suggested that workmen in the cereal grain storage and transporting industry are at risk of developing obstructive pulmonary disease and because farmers are exposed to grain dust, they too may be at risk.

Mastroangelo et al (1984) reported on a cross-sectional study on chronic respiratory disease among farmers: A total of 2,932

farmers (90.9% response rate) was studied in an attempt to ascertain the prevalence of respiratory disease and the various associated factors. A 10% random sample of this population was then compared with a sample of tradesmen and clerks living in the same area. A questionnaire was used to obtain information about respiratory symptoms and various risk factors, a chest radiograph was taken, and forced expiratory volume in 1 s ($FEV_1$) and forced vital capacity were measured. After the first screening the transfer of carbon monoxide, allergic skin tests, and precipitin tests of the sera were performed. Chronic bronchitis was significantly more frequent among the farmers than among the referents (9.9 vs 4.8%). The prevalence of bronchial asthma was similar in both groups (2.8 and 2.4%)> The $FEV_1$ was lower among the farmers. The prevalence of farmer's lung was 1.4% for the farmers, whereas no such disease was found in the reference group. The risk of chronic respiratory disease appeared important only on small farms and in traditional stables, linked to a farming method that is being replaced.

A clinico-epidemiological study was done by Tsiura et al (1984) in 913 adults, 332 teenagers, and 518 children - inhabitants of a number of districts of the Leningrad region. The study was based on a questionnaire compiled in accordance with the WHO requirements; general checkup; roentgenological examination; external respiration tests. The incidence of chronic non-specific lung diseases among milkmaids was 20.3%, among pig-tenders 29.8%, among poultry-women 31.5%, among machine-operators 34.3%, among vocational school students 10.4%, among children 10.7%. The results of the checkups demonstrated a possibility of and a need for an early active identification of the initial, asymptomatic stages of chronic, non-specific lung diseases, with the view of providing dispensary services for such persons and conducting follow-up prophylactic examinations.

Gylseth et al (1984) analysed mineral particles in lung tissue from a farmer who underwent lobectomy due to a lung tumor and related these findings to occupational exposure and histopathological and clinical diagnoses. Despite no clear evidence of previous occupational dust exposure, heavy deposits

of birefringent particles and slight pulmonary fibrosis were found during histopathological examination. Extracts from the lung tissue were analyzed by electron microscopy and X-ray microanalysis for mineral particles. The major components of the dust were identified as mica, talc, and silica. Minor components included asbestos fibers and rutile fibers. Some of these fibers were coated by ferroproteins. Mica, quarts, feldspars (plagioclase), and rutile fibers were found in the soil from the farmer's potato storehouse. Based on these findings it is assumed that the slight pulmonary fibrosis is probably caused by the different mineral particles deposited.

A retrospective study of hospital visits was reported by Pratt and May for farm-associated lung injury in rural Otsego County, New York during an 11-yr period. Twenty-two males and 1 female experienced a total of 26 episodes of illness. Eighty-four percent of the episodes occurred between July 1 and October 31. Four of the 23 individuals died, 2 acutely and 2 after a slowly progressive, debilitating disease. One patient died of suffocation in a silo; 2 patients had silo filler's disease, 1 dying acutely. Of 6 patients with farmer's lung disease, 2 died of progressive fibrosis. The remaining 4 patients suffered an acute febrile illness typified by short duration, clear chest radiograph, and negative serologies. They refer to this as "Silo Unloader's Syndrome" and conclude that it is a more common occurrence in the farm environment than some of the more known disorders. This study demonstrates that occupational lung injury is a problem affecting a young (average age 36 yrs) vigorous population with potentially fatal consequences.

Neukirch et al (1983) studied the mortality due to respiratory disease in France between 1970 and 1974 as well as in seven other countries in the European Economic Community. The French results were presented as an index of mortality by cause of death, enabling a comparison of the mortality in different groups of the population. Data was supplied for 7 diagnostic groups defined according to List A of the International Classification of Diseases. The population studied consisted of men and women between 15 to 64 years, classified according to residence (urban

or rural) and profession (agricultural worker or not). In addition the indices of mortality for farmers or agricultural employees were compared to men of the same social class, for the same period.

The comparisons between the urban and the rural background revealed an excess mortality for respiratory tuberculosis, lung cancer, bronchitis, emphysema and asthma for respiratory diseases in both men and women; this was also found comparing agricultural to non-agricultural workers. Lastly, if one compared agricultural and non-agricultural workers of the same social class, deaths due to acute and chronic respiratory infections were higher in the agricultural workers. These results show the relative importance already stressed in other studies, of acute respiratory diseases in agricultural workers.

Heller and Kelson (1982) reported a co-operative study by representatives of eight member countries of the EEC into the problem of respiratory disease among agricultural workers. From each country mortality data (routinely collected but often unpublished) were obtained for seven disease categories in the country as a whole, and separately where possible for urban and rural areas, and agricultural workers. The results indicated that comparable data can be collected from different countries despite variations in local methods of data collection and coding. There are large between-country differences in respiratory disease mortality rates, and data for agricultural workers in France and England and Wales suggest an excess of acute respiratory disease deaths (mainly pneumonia and influenza) among agricultural workers.

Dean (1982) reports that the relative frequency of respiratory disorders in farmers indicated the need for further examination of occupationally induced respiratory disease among agricultural workers. This need has resulted in a study supported by the Directorate-General for Employment and Social Affairs of the EEC. The study has been undertaken in three ways. In Ireland, studies on farmers' lung and other respiratory diseases among farmers have continued. In France, studies on obstructive airways diseases in agriculture workers in Normandy are being undertaken

to ascertain mortality from respiratory disease and non-rheumatic heart disease comparing the countries of the Community excluding Luxembourg. This latest study is being undertaken under the guidance of a steering committee.

An epidemiological survey of pollenosis on 96 farmers engaged in a pear orchard in Toyama prefecture was carried out by Teranishi et al (1982). All subjects were asked about the complaint of clinical manifestations from pollens and examined by the intradermal skin test with pollen extracts. Airborne pollens were collected in the pear orchard using a gravity sampler.

The results suggested that the pear farmers were exposed to the pollen grain of japanese pear and annual bluegrass, and pollen allergens sensitized them inducing nasal and or ocular symptoms.

Shelley and Ward (1981) undertook a survey to assess the prevalence of respiratory symptoms among young farm workers and to provide guidelines on the extent to which young farmers in Ireland are occupationally exposed to causes of respiratory disease. The study was carried out during the annual conference of the young farmers' association in 1979.

Cuthbert (1981) surveyed fifty farming families on the mainland (the largest island) of Orkney to assess the amount of allergic respiratory disease and the principal causative factor. This account deals with only type 1 allergy and demonstrates a prevalence of asthma and rhinitis of 17.3% and of extrinsic asthma and rhinitis, in which definite allergic causes can be identified, of 12.7%. In addition it is shown that over one-fifth of the farming community are 'atopic' in that they demonstrate positive prick tests to one or more allergens. Less than 50% of those with allergic respiratory disease have attended the doctor with their complaint, a fact which calls in question the validity of epidemiological studies of allergic desease based on hospital and clinic attendances. Sex distribution confirms the finding that males suffer from asthma more frequently than females, however more females than males give positive skin tests

without exhibiting symptoms of allergy. Pollens, animal danders and fungi all have a part to play in the aetiology of asthma and rhinitis among Orkney farmers, although the incidence of grass pollenosis is well below average. The two commonest allergens are hay dust and Dermatophagoides pteronyssinus which are found frequently to affect the same subject.

Asthma and rhinitis are described in a paper by Cuthbert et al (1979), and not farmer's lung, in a farming population due to the non-pyroglyphid grain storage mite. Before a diagnosis of farmers' lung due to mouldy hay is made in any patient whether or not precipitins to Micropolyspora faeni are present, skin tests for storage mite should be made. If these are positive a diagnosis of 'barn allergy' should be considered and a trial of sodium cromoglycate be given.

Sherwin et al (1979) reported on abnormal numbers of birefringent particles found in the lungs of seven patients (five vineyard workers, one farmer, and one rural resident) in association with a spectrum of early to late interstitial inflammation and fibrosis. Nodular granulomas of the types seen in silicosis were absent. Scanning electron microscopy and energy dispersive x-ray analysis of 177 individual particles (less than 5um.) in situ in the lungs of four of the patients showed mostly silicates (notably aluminum, silicon, and potassium), with 5 to 10 percent silicon dioxide. An analysis of particles less than 5um. from both vineyard and non-vineyard soil showed lung and soil particles to have a similar composition. The presence of large amounts of silicates in the lung tissues, in asssociation with chronic inflammation and fibrosis, implicates the silicates in the causation of the fibrosis. The silicate deposits may, in large part, be a marker, reflecting a mixture of toxic soil additives or pesticides found in commercial clay silicate products or in dusts from the soil itself. The findings do not exclude lung pathology of a similar nature in regions outside of the farm.

Dutkiewicz (1978) performed microbiological examinations of the air in grain storing and processing plants and in animal

houses. Large concentrations of viable microorganisms, ranging from 129.2 to 1289.9 thousands/m3 of air, were found in the rooms contaminated with grain dust and much lower in those contaminated with flour dust (22.6 thousands/m3). Bacteria predominated in the air of grain plants, whereas actinomycetes and fungi were less numerous. The most abundant bacteria were Gram negative rods of the species Erwinia herbicola.

Large concentrations of air-borne microorganisms were also found in different animal farms, reaching 22.5 to 595.4 thousands/$m^3$ in hatcheries and 7751.5 thousand/m3 in a broiler house. Staphylococci were most frequently isolated and other common organisms were corynebacteria and streptococci. It was concluded that high exposure to dust-borne bacteria creates a hazard to agricultural workers.

Dutkiewicz (1978) performed immunological tests (agar-gel precipitation, complement fixation, passive cutaneous anaphylaxis, and intradermal) with the extracts of these bacteria in different groups of grain workers and in other groups of population. Tests with extracts of grain dust and other micro-organisms were also performed.

Grain workers showed in all the tests a high incidence of positive reaction to E.herbicola, being significantly higher, as compared with unexposed subjects. Different actinomycetal and fungal extracts gave lower percentages of positive reactions. Skin reactions to E.herbicola were significantly correlated with the reactions to grain dust and showed a close relationship with the degree of exposure. The grain workers with respiratory symptoms reacted more frequently to E.herbicola than asymptomatic ones, both in intradermal and precipitation tests. Thus, these bacteria should be considered as a factor increasing risk of the respiratory disorders among grain handlers.

Zolov et al (1967) presented the results of fluorographic examination of 3325 persons in the rural region of Avren (South Bulgaria) living within 10 km of an asbestos mine. This demonstrated 155 cases of pleural asbestosis. Of these, only 23 were engaged in the production or transport of asbestos, while

the remaining 132 persons (86 men and 46 women) had had no occupational contact with asbestos. The majority (71.6%) were agricultural workers over 50 years of age, occupied primarily in tobacco production. Studies of environmental conditions, as well as the limited scope of underground work (only initiated in 1942), the age distribution of cases, and the conditions of the agricultural work (cultivation of tobacco in stony ground containing asbestos minerals) lead to the conclusion that their observations are not those of 'endemic asbestosis' in the sense of being caused by air pollution derived from mine dust alone, but of a unique occupational asbestosis in agricultural workers in the region studied.

Cohen et al (1967) presented a case of a sawmill worker with a long and heavy exposure to redwood sawdust who had chronic pneumonitis with foreign body granulomas associated with the alveolar-capillary block syndrome. Histologic evidence suggests that deposits found within the granulomas are endogenous siderocalcific encrustations upon minute dust particles, similar to those encountered in farmer's lung disease. The patient's serum contained more antibodies against redwood extracts than did the serum of similarly exposed workers, and he reacted to at least one antigen in redwood sawdust against which no other subject reacted. Two fungal species encountered in redwood dust contained antigens immunologically related to the redwood dust antigen against which only the patient's serum reacted. The similarity of this condition to farmer's lung disease, maple bark disease and bagassosis is discussed. It seems likely that this patient's pulmonary injury resulted from reaction to ispired redwood dust or fungal particles.

Pulmonary granulomatoses due to inhaled organic antigens were reviewed by Rankin et al. Numerous granulomatous disorders may produce diffuse or localized pulmonary lesions. Moreover, a similar histologic appearance may be observed in several seemingly unrelated diseases. The list of agents capable of producing epithelioid granulomas (tuberculoid granulomas) has always been a long one, including mycobacteria, fungi, protozoa, beryllium, and zirconium. To this list must now be added several

organic dusts of animal or vegetable origin. During the past decade clinical and laboratory investigators have repeatedly demonstrated that a diffuse granulomatous pneumonitis may result from the inhalation of organic dusts by persons who have become sensitive to antigens in the dusts.

Farmer's Lung

Terho et al (1984) studied the occurrence of symptoms suggestive of farmer's lung among the immediate relatives of 37 patients with clinically established farmer's lung, among the 36 immediate relatives of the patients' spouses, and among unrelated persons (spouses of relatives). Symptoms of farmer's lung had occurred about twice as frequently among the relatives of farmer's lung patients as among the subjects in the other study groups. The results, supported by findings from earlier studies, imply that genetic factors may be involved in pathogenesis of farmer's lung.

Cuthbert et al (1984) undertook a study to determine the prevalence of disease due to storage mites among farmers on the mainland of Scotland. Of the 290 subjects employed on 102 randomly selected farms studied, eighty-seven (30%) reported allergic symptoms on entering barns or byres, and prick tests to storage mites were positive in 62 (21%). Rhinitis and conjunctivitis together were the more frequently reported symptoms, with less than half the subjects reporting allergic symptoms associated with hay dust. Specific IgE to storage mites was strongly associated with atopy in those subjects who reported allergic symptoms.

Terho et al (1983), using preset uniform criteria, collected data from all pulmonary disease units in Finland. There were 186 new cases of FL in 1980. The mean age was 46 years, and 64% were women. Using the national population 1975 as standard, the rates were standardized for age and sex. There were differences both in the incidence and in the sex ratio of FL among the farming

population of the six districts of Finland. These differences are closely related to prevalent proportions of cattle raising among farmers and local cultural traditions in the various districts. Seasonal variation in the incidence of FL was statistically significant (Roger's test, $p<0.001$), the peak occurring in April. This confirms an earlier observation. The incidence rates were statistically significantly correlated with the sum and mean of daily rainfall during the haymaking period preceding the diagnosis of FL.

Cuthbert and Gordon (1983) asked 29 patients previously diagnosed as having suffered from farmer's lung in or before 1970 whether the condition had recurred and what measures they had taken to avoid such recurrences. Those who had retired from farming had been least affected by recurrence, while those who continued to farm had been protected by making silage instead of hay or by wearing protective respirators. To be effective, a respirator should be worn on every occasion that farm dust is encountered and must be properly maintained.

Lacey et al (1982) tested respirator filters marketed for protection against agricultural dusts for their ability to retain actinomycete spores implicated in farmer's lung disease. Because mixed cultures gave variable estimates, media selective for Thermoactinomyces spp., mostly T.vulgaris Tsiklinsky (spores 0.6-1.0nm dia.) were used. Thermoactinomyces spores penetrated all filter types: up to 44% through nuisance dust filters, 3% through cartridge filters to British Standard BS 2091 Type A standard, 0.3% through BS 2091 Type B standard cartridges, 0.1-3.1% through different types of filter for a ventilated helmet and 0.5% through a powered positive-pressure respirator. The best disposable filtering face masks also allowed about 3% mean penetration but there was considerable sample to sample variation. Filters to BS 2091 Type B standard have been recommended for protection against farmer's lung but research on dose-response relationships is needed to determine whether 99.7% retention of spores is sufficient to prevent sensitization or disease.

Seal et al (1982) described the pathology of five patients who had a biopsy in the acute stage; interstitial pneumonia, sarcoid-like granulomata, bronchiolitis, and vasculitis were found. Three of these patients progressed to the chronic stage, when the one with the most extensive bronchiolar involvement had lung function findings of airway obstruction. One progressed to the chronic stage with lung function findings of a transfer defect, and another had radiographic evidence of pulmonary fibrosis with normal lung function tests at rest. The pathology of the chronic stage is described in six patients, with necropsy findings in five. Interstitial pulmonary fibrosis, cystic change, and pulmonary hypertensive changes were the principal findings.

Terho et al (1982) performed qualitative and semi-quantitative microscopic analyses on the mite populations in dust samples collected from the byres and hay and grain storages of 11 farms in Eastern Finland. Storage mites were found in all farms. The mite fauna was more abundant in the byres and hay storages than in the grain storages. The most common species of general were Acarus siro, Acarus farris, Glycphagus domesticus, Lepidoglyphus destructor, Cheyletus eruditus, Tydeus spp., and Tarsonemus spp. The results imply that also in northern climates storage mites should be considered as possible causes of allergic disorders among farming populations.

Gruchow et al (1981) studied the prevalence of farmer's lung disease and antibodies to farmer's lung antigens in a probability sample of over 1,400 farmers in north central Wisconsin. The prevalence rate of farmer's lung disease was 4.2 per 1,000 farmers. The most prevalent antibody type was directed against Micropolyspora faeni, with 6% of the study population precipitin-positive. Prevalence of antibodies to M.faeni was associated with dairy farming, larger farms, and larger dairy herds. An additive effect of hay acreage and size of dairy herd was observed. An independent relationship was also observed for cigarette smoking, with antibodies to M.faeni more prevalent among nonsmokers.

Edwards and Davies (1981) have shown an immunologic basis for episodes of farmer's lung by the response of susceptible individuals to inhalation challenge with extracts of Micropolyspora faeni, the main sensitizing agent in mouldy hay dust. However, if the complement-fixing capacity of the farmer's serum for M.faeni is used and a quantitative assessment of sensitivity, it does not predict whether an individual will respond to inhalation challenge. A positive immediate skin test to M.faeni antigens was observed in all cases with over 40 CH50 consuming units of antibody per milliliter of serum. A similar correlation was seen between complement consumption and precipitins.

Warren (1981) administered to a group of 76 cattle farmers from southern Manitoba the National Heart, Lung, and Blood Institute questionnaire on respiratory symptoms and supplementary questions of farming and farming-related symptoms. Lung function was tested, serum was examined for precipitating antibodies, and skin testing with common allergens was performed. Analysis of the men's answers revealed a high prevalence of chronic respiratory symptoms among the farmers in all categories of smoking history, and the presence of these symptoms was significantly associated with a history of symptoms related to handling mouldy hay or grain; 51% of the men had chronic symptoms and 55% had symptoms related to crop handling. In seven farmers, (9%) the symptoms related to crop handling suggested an attack of farmer's lung. One other farmer, with a history of illness after handling mouldy hay, had a reduced total lung capacity, and in 18 the ratio of the forced expiratory volume in the first second to the forced vital capacity was lower than predicted. Precipitating antibodies against thermoactinomyces were absent in all farmers, but two farmers had antibodies against aspergillus ruber. Immediate hypersensitivity was found in 16 (21%) of the farmers; sensitivity to dermatophagoides farinae was commonest.

Siracusa et al (1981) presented 17 cases of farmer's lung with particular regard to clinical, radiographic, lung function and serological characteristics. Based on the criteria adopted, an acute form was diagnosed in 8 subjects, a chronic form with

acute onset in 6 subjects, and a chronic form with insidious onset in 3 subjects. On the basis of the available literature, the authors believe that the incidence of farmer's lung in Italy is underestimated, due to the insufficient knowledge of general practitioners, who are the first, and often the only ones, to observe the characteristic clinical features of the disease in its acute phase.

Hendrick et al (1980) assessed the validity of inhalation tests in the investigation of extrinsic allergic alveolitis from the results of 144 antigen and control tests in 31 subjects. A definitive pattern of positive late responses was observed. Reactions to nebulised bird serum and droppings in subjects with bird fancier's lung were identical to reactions after 'natural' exposures in aviaries or lofts, and to reactions after 'occupational' challenges in subjects with farmer's lung and mushroom worker's lung. In general positive tests were easily recognised subjectively from symptoms and signs appropriate to an influenza-like illness and undue respiratory effort on exercise. They were associated with significant changes in six readily available objective monitoring measurements - exercise minute ventilation, body temperature, circulating neutrophils, exercise respiratory frequency, circulating lymphocytes, and forced vital capacity. These confirmatory monitoring tests had specificities of approximately 95% and sensitivities of 85-48%. Measurement of diffusing capacity, lung volume subdivisions, or resting minute ventilation/respiratory frequency proved to too insensitive to be useful, as did auscultation and chest radiography. We conclude that responses that do provoke significant changes in these less sensitive tests are unnecessarily distressing and, presumably, unnecessarily hazardous.

The respiratory status of a sample of Vermont male dairy farmers was reviewed by Babbott et al (1980), and a comparison group from industy, matched for age, sex and smoking. Survey instruments included a standardized questionnaire and simple pulmonary function tests. In general, past and present smokers had more respiratory symptoms than never-smokers; and farmers, in

all smoking categories, reported symptoms with greater frequency than did their counterparts from industry. Forced vital capacity (FVC) tended to be lower among men with a history of smoking but, within each smoking category, dairymen and factory workers had very similar FVC's. Farmers who had never smoked or who were current cigarette users had lower $FEV_1$/FVC rations than their controls from industry. Sixteen dairymen demonstrated precipitins to either micropolyspora faeni or Thermoactinomyces vulgaris, but only one reported a constellation of symptoms compatible with farmer's lung disease. The estimated prevalence of antibodies to thermophilic actinomyces in this farm population was approximately 10 per cent. Although sample sizes were limited, dairymen from small farms tended to be older, have more respiratory symptoms, less satisfactory pulmonary function, and more serologic evidence of exposure to farmer's lung antigens than their counterparts from large farms.

Terho et al (1980) investigated the seasonal variation in the incidence of 78 consecutive cases of farmer's lung according to a statistical method described by Roger. The cyclic trend was statistically highly significant and the centre of gravity of incidence appeared in the latter half of April.

Cuthbert et al (1980) undertook to compare the IgE levels to specific storage mites in the sera of five farming and one control subject, with the numbers of mites present in their hay. Samples of hay were collected at monthly intervals and the total number of mites per gram of hay in each sample recorded. Blood samples were also taken at monthly intervals from all the subjects and assayed by radioallergosorbent test for specific IgE to five storage mite species and to the house dust mite (Dermatophagoides pteronyssinus). Mite numbers, both in respect of total counts and specific estimates, showed a rapid increase to a peak during the month of October with a subsequent fall in November and a partial recovery in December, after which numbers tended to even out. Only two of the farmers showed consistently raised levels of specific IgE to any of the storage mite species and these tended to follow the fluctuations of the mite numbers during the months to January 1978, after which one farmer showed

a fall in positive IgE titre to T.longior, whilst the other who was positive to A.farris showed a sudden rise in titre to this species.

Wells (1980) did a review on farmer's lung for the Farm Safety Association (of Ontario) and concluded:

1. The possibility of farmer's lung should be considered in any farm worker suffering from breathlessness without evidence of cardiac failure or airways obstruction.

2. Farm workers who have acute reaction to the fungal spores upon exposure, are often diagnosed as suffering from pneumonia. In many instances, it is only after a lengthy attempt at treatment, are other causes (and treatments) considered. Yet, an acute case of farmer's lung is not difficult to diagnose, provided a proper history is taken.

3. Subacute response to the spores is rarely diagnosed. This insidious form of the disease, with antibodies still present 3-4 years later, is estimated to occur in 20-40% of farm workers.

4. The effect (additive, synergistic, antagonistic) of an earlier exposure (e.g. autumn exposure to silo gas followed by a winter exposure to the fungal spores) to silo and/or manure gas at a subacute or acute level, on a worker who is sensitive and exposed to the allergens implicated in farmer's lung, appears not to have been evaluated. When one considers that those who are most likely to be exposed to the farmer's lung allergens also have a high degree of potential exposure to silo and/or manure gas (beef, dairy or pork producers), this becomes more critical.

5. Evaluation of the prevalence of farmer's lung (acute or subacute cases) among the Ontario agricultural community has not been done. Special concern may be expressed about those who are sensitive to the allergens but have a subacute response on exposure. If undiagnosed and chronic exposure continues, increasingly severe, irreversible fibrosis can occur.

As a result he has recommended that physicians serving the rural farm community must be made aware of farmer's lung - when to expect it, clinical presentation, and diagnostic tools. Also farm workers must be made aware of the potential health hazard associated with contact with moldy vegetable materials.

Information on symptoms, prevention and protection must also be made available to them. The effect of a prior exposure to silo and/or manure gas on a worker, sensitive to farmer's lung allergens, needs to be evaluated. As well a study on the prevalence of the disease in the Ontario agricultural community should be conducted. Special emphasis should be directed at identifying the proportion of farm workers who have never had the classical illness (but have had a subacute response) and yet have antibodies.

Braun et al (1979) evaluated 141 patients with farmer's lung disease to determine its long-term effects and factors influencing the outcome. At the time of the last follow-up, 29 patients had died and 92 (mean age, 54 years ) were studied clinically, physiologically, and radiologically. The mean length of disease was 14.8 years (range, 2.25 to 40 years). Symptoms at the time of the last follow-up included complaints of cough (33 percent of the patients), breathlessness while walking on the level (20 percent), breathlessness on minor exertion (14 per cent), and breathlessness while at rest (3 percent). Twenty-eight percent had chronic bronchitis. Thirty-nine percent (36 of 92 patients) had some evidence of interstitial changes on roentgenogram. Abnormal vital capacity was present in 11 patients (12 percent), abnormal total lung capacity in 11 (12 percent), and abnormal CO diffusing capacity in 27 (30 percent). The ratio of one sec forced expiratory volume to forced vital capacity was abnormal in 23 patients (25 percent), and arterial $Po_2$ was abnormal in 39 (40 percent). Patients with a history of 5 or more symptomatic recurrences had significantly smaller values ($P<0.05$) for vital capacity, total lung capacity, and CO diffusing capacity than did those patients with less than 5 recurrences. There was no significant relation between continued farming or length of disease and lung function. On the basis of several measurements of airway function, 34 of the patients (58 percent) were found to have some abnormality. It is concluded that symptomatic recurrences may be the most important factor in determining the danger of progressive disease. Persistently positive precipitins were correlated with decreased CO diffusing capacity. Moreover, airway disease is relatively uncommon, but

does occur, and in some cases it is a possible consequence of farmer's lung disease.

Ingram et al (1979) reported that in an investigation of the relationship between storage mites and symptoms of allergic respiratory disease in farmers exposed to hay and grain dust, the clinical responses suggested an immediate type-I hypersensitivity. This study confirmed that farmers are exposed to large numbers of mites, particularly while feeding cattle. Storage mites may be an important cause of asthma in the farming community and should also be considered in the differential diagnosis of farmer's lung.

Edwards (1979) observed that the soluble material derived from the respirable fraction of mouldy hay dust has anti-complementary as well as enzyme activity. It is probable that the capacity to activate C1 resides in other dusts and may be a basis for non-immune histamine release in the lungs when such a dust is inhaled. It is also probable that non-specific skin reactions are related to C1 activation. The finding of an enzyme with papain-like activity is significant since the introduction of papain into the lungs of the experimental animal leads to emphysema and this has been described as a feature of farmer's lung.

Bureau et al (1979) reported a five-year-old child with classic farmer's lung disease. The disease started after a flulike episode and progressed during three months to severe respiratory failure. The clinical features were fatigability, weight loss, recurrent fever, dry cough, pulmonary rales, and clubbing. Serological studies for precipitins to Micropolyspora faeni were positive. The chest roentgenogram showed a ground-glass appearance with air bronchogram. The open lung biopsy material was typical for alveolitis, with minute interstitial granulomas and obliteration of lung parenchyma. The child's condition improved rapidly with prednisone therapy and avoidance of the allergen.

Gump et al (1979) surveyed several Vermont population groups for the occurrence of antibodies to thermophilic actinomycetes. Antibodies to M.faeni and T.vulgaris were measured by the precipitin method in all subjects and, in 124 subjects, M.faeni antibodies were also measured by the indirect fluorescent antibody (IFA) technique. There was relatively good correlation between the two techniques (r.0.48,p<0.01). Hospital employees, blood donors and patients with chronic bronchitis were generally negative for precipitins to thermophilic actinomycetes. Of the 258 Vermont dairy farmers surveyed, 14 (5.4%) had precipitins to M.faeni, 3 (1.2%) had precipitins to T.vulgaris but only 1 farmer with antibodies to M.faeni had symptoms of possible farmer's lung disease. On the other hand, 10 (4.1%) preciptin-negative farmers had symptoms possibly consistent with FLD. The IFA test did not correlate any better with symptoms. Seven (5.6%) patients with pulmonary fibrosis had precipitins to M.faeni; five of these were diagnosed as having FLD. Eighteen (14.4%) had precipitins to T.vulgaris and only 3 of these patients were felt to have hypersensitivity pneumonitis. Patients with pulmonary fibrosis and FLD had IFA titers of >1/128, but so did asymptomatic farmers.

Katila and Mantyjarvi (1978) studied precipitating antibodies towards antigens associated with farmer's lung disease in Finnish dairy farming and non-farming rural populations and the results were compared to those of serum samples of patients suspected of having a fungal allergy. The antigen panel consisted of Aspergillus fumigatus, Micropolyspora faeni and Thermoactinomyces vulgaris. All three microbes seemed to be important environmental inducers of antibody formation. The prevalence of antibodies towards all of them was higher in the patient group. The presence of A.fumigatus and T.vulgaris antibodies correlated best with the occurrence of respiratory disease. The difference in M.faeni antibody prevalence between patients and the control group was less significant.

Marx et al (1978) evaluated farmers for the presence of farmer's lung disease by serologic methods and by clinical histories. From a large farming population screened

serologically, 40 of 92 farmers with precipitating antibodies to the thermophilic actinomycetes consented to be evaluated for clinical evidence of farmer's lung disease. Each subject completed a standardized questionnaire which was reviewd by a trained observer. On the basis of the questionnaire and an indepth clinical history, the subjects were grouped into those farmers who had a history of farmer's lung disease (38%), those with no history (50%), or a doubtful subgroup (12%). When these groups were compared for radiologic changes, pulmonary function abnormalities, and immune function, no differences were discernible. None of the parameters tested were useful in predicting which farmer would develop clinical farmer's lung disease. The parameters tested did not provide reliable criteria for differentiating those patients who present without acute symptoms but relate a history of recurrent pulmonary illnesses associated with mouldy forage.

Wardrop et al (1977) studied the microbiology of the air of byres and bruising sheds and of hay, grain and dust from bruising machines in 12 dairy farms in Ayrshire and one in Perthshire. Seven farms (FLD) had a known case of farmer's lung disease and five farms (non-FLD) were free from the disease. Concentrations of mesophilic organisms and of thermotolerant and thermophilic fungi did not vary significantly between the two types of farm but the concentrations of thermophilic actinomycetes and bacteria, notably Micropolyspora faeni, were higher in general on FLD farms. Culture filtrate and mycelial extracts of the most commonly isolated organisms were tested against three groups of sera (11 from patients with farmer's lung disease, 14 from healthy personnel on FLD farms and 13 from personnel without farmer's lung disease on non-FLD farms. Sixty nine percent of seropositive personnel on FLD farms were also symptomatic apparently correlated with the higher concentrations of M.faeni encountered on FLD farms.

Marx et al (1978) measured complement-fixing antibodies (CFA) to a panel of microoganisms commonly associated with respiratory disease in a number of agricultural populations. The panel

included a variety of pathogens.

Madsen et al (1976) surveyed 471 persons associated with farming or dairy production by means of a questionnaire for evidence of hypersensitivity lung disease due to inhalation of mouldy hay or grain (farmer's lung). Of these, 172 were evaluated with spirometry, serologic studies, and chest roentgenographs. A history typical of the farmer's lung syndrome was given by 14 of the 471 subjects (3.9 percent). Precipitating antibodies to Micropolyspora faeni were identified in sera from 2 of these 14 subjects (14 percent), and spirograms were abnormal in 4 (28 percent). The prevalence of farmer's lung in this community (i.e.3 percent) is comparable to that found in epidemiologic studies in Britain and Scotland. Farmer's lung disease may be an important occupational illness of dairy and cattlemen in this country, but the diagnosis may be overlooked frequently because of the lack of patient and/or physician awareness.

Morgan et al (1975) carried out surveys on random samples of the farming population in Devon and Wales in order to estimate the prevalence of respiratory symptoms and of positive precipitin reactions to thermophilic fungi. Bronchitis, as defined, was common among the Welsh hill farmers, and the proportion of positive serological tests was higher in both the areas surveyed in Wales as compared with Devon. All three surveys confirmed a previous finding that the proportion of positive precipitin tests was higher among non-smokers according to the presence of absence of positive precipitin tests. The difficulty of determining prevalence rates for farmer's lung is discussed, but the results suggest a rate not dissimilar to those found in two areas of Scotland which were more than 20 times higher than any figure previously reported in Britain.

Fukal et al (1974) reported that microscopic pulmonary changes in the acute phase of farmer's lung may be characterized as a diffuse interstitial granulomatous pneumonitis, while during the chronic phase the signs may be found indicating a diffuse interstitial fibrosis, respiratory fibrotic alveolitis. Problems

concerned with differential diagnosis of acute and chronic phases of the disease are discussed.

Some lung function tests were made in five patients with different stages of farmer's lung by Mayer et al (1974): three were in an acute phase of the disease, two of them had recovered from the first episode. Diagnostic lung biopsy was carried out in one of these two patients, the second patient experienced four acute attacks during the period of four years which resulted in significantly decreased values of lung diffusion capacity for CO, although respiratory capacity remained within the normal values. Prolonged exposure to mildew organic dust induced very serious clinical symptoms with right heart failure in a 61 years old male patient. Corticoid therapy in this patient gradually improved respiratory capacity, blood gases values as well as diffusion lung capacity. Another two patients exhibited symptoms of a chronic disease. Diagnostic lung biopsy was performed in a female patient with clinical symptoms of an obstructive ventilatory dysfunction with reduced respiratory capacity. The last case showed symptoms of an obstructive ventilatory dysfunction with decreased diffusion lung capacity.

Minarik et al (1974) used five selected cases of the farmer's lung type fibrotic alveolitis to demonstrate that different degrees of fibrosis may be detected in the lungs already in the early stages of the disease. If the exposure persists, fibrotic changes become progressive and may be objectively diagnosed even without biopsy, in dependence on their extent and the sensitivity of the functional tests used.

Patterson et al (1974) presented a case where after a latent period of three weeks following an intense inhalational exposure to mouldy corn, a farmer developed pneumonitis apparently of a hypersensitivity pneumonitis type. This illness was associated with serum precipitating antibodies against antigens in the mouldy corn and against antigens of Aspergillus flavus and fumigatus. The former organism was cultured from the mouldy corn and precipitin bands of identity between an extract of mouldy

corn and aspergillus antigen were demonstrated using the patient's serum. Organizing bronchiolitis obliterans was found in pulmonary tissue after death occurred, the latter presumably due to pulmonary embolism. This case is believed to represent the occurrence of hypersensitivity pneumonitis following massive inhalation of the spores of the genus A.flavus possible with transient respiratory infection with these organisms but without systemic invasion of the host.

Morgan et al (1973) carried out a survey in Devon among 91 farmers and their families in order to estimate the prevalence of respiratory symptoms and of positive precipitin reactions to thermophilic fungi. Answers to a questionnaire about respiratory symptoms and smoking habits revealed among the men a prevalence of symptoms comparable with those found in other surveys of agricultural populations in the United Kingdom but with a lower proportion of smokers. A positive answer to a question about attacks of breathlessness associated with fever or shivering appeared to differentiate people suffering from farmer's lung. Twenty-three percent of the population had precipitins to Micropolyspora faeni and two of these individuals also had precipitins to other fungi. There were statistically significant differences in the proportions of positive precipitin tests found in smokers, ex-smokers, and non-smokers. Six known cases of farmer's lung were included in the sample and all had positive precipitins.

Grant et al (1972) reported on a survey of the farming population of Orkney, Ayrshire, and East Lothian the prevalence of farmer's lung was estimated 86 per 1,000 in both Orkney and Ayrshire and 23 per 1,000 in East Lothian. If cases with a negative farmer's lung hay (FLH) precipitin test are excluded these figures are reduced to 43, 36, and nil respectively, but those for Orkney and Ayrshire are still about 20 times higher than any figure previously reported for the prevalence of farmer's lung in Britain. Regional variations in prevalence are probably related both to climatic conditions and to differences in agricultural methods, the latter often being dictated by economic circumstances. Nevertheless the prevalence of farmer's

lung could be reduced considerably by the energetic application of preventive measures, backed by financial incentives. The most important of these are efficient drying of hay and cereals before storage, more extensive use of silage, better ventilation of farm buildings, and the introduction of mechanical feeding systems. Individual farmworkers would be taught how to recognise the early symptoms of the disease and encouraged to wear respirators when handling mouldy fodder.

Nash (1970) reported a case of irreversible lung damage and cor pulmonale in a hypersensitive subject exposed to pigeon dust for many years. A 63-year-old white female was referred to the Cardiac Clinic, Groote Schuur Hospital, for investigation of her cough and shortness of breath. The patient dated the onset of her symptoms to an attack of 'bronchitis' in 1963, 5 years previously; following that episode, her cough persisted with the production of yellow sputum in the mornings only with no haemoptysis. The patient had never smoked cigarettes. Her husband had been an enthusiastic pigeon-fancier for over 18 years and she had often helped him by feeding the birds, sitting in the loft for long hours during the process.

Hapke et al (1968) observed that in assessing patients suffering from farmer's lung, the acute stage must be distinguished from the chronic stage of the disease. The conspicuous radiographic signs in the acute farmer's lung episode and the often dramatic clearing make an important contribution to the diagnosis. The radiographic changes in chronic farmer's lung are not specific and cover a wide range of appearances. Even minor nodular changes are significant. Farmer's lung, acute and chronic, is not a disease predominantly characterized by a defect in gas exchange. During the acute illness the reduction in diffusing capacity is often accompanied by a decrease in lung volumes; the pulmonary function profile of the chronic stage is variable. In only a relatively small proportion of chronic farmer's lung patients does a defect in gas exchange predominate, and in some it may be manifest only during exercise. Airway obstruction is a feature of chronic farmer's lung. In chronic

farmer's lung patients, discrepancies between the severity of complaints and results of pulmonary function tests are not infrequent. In some patients with considerable disability conventional pulmonary function studies may demonstrate little or no impairment of the functions measured. In patients suffering from an acute farmer's lung episode, serological tests should be positive, possibly in high titre. In the chronic stage of the disease, the chance of finding positive serology in a patient diminishes with the length of time elapsed since the last acute episode. The period of serological transition appears to be the third year.

## Silo-filler's Disease

In a brief to the Ontario Task Force on Health and Safety in Agriculture Lees (1984) reported on silo hazards and safety, stating that silos constitute the major site of non-transport accidental farm fatality. Silos are a common feature in Ontario farms. While many farmers profess to be aware of the danger of silo entry, most admit to ignoring the safety procedures which should be exercised during entry. It is questionable how widespread the knowledge of danger really is in view of the frequency with which a second man will follow one who has collapsed within the structure.

There are two main types of silo on our farms - the modern airtight unit (Harvestore type) and the traditional tower silo which is similar in shape to the former but is not sealed. In the Harvestore type of silo, fermentation of corn produces carbon dioxide, consuming the available oxygen in the process. Within a short period of time there may be no detectable oxygen within the unit. A person entering the silo loses consciousness almost immediately, so quickly in fact that he is probably incapable of saving himself even if he recognises he is in trouble.

The hazard in the non-airtight tower silo is different. Degradation of the silo contents produces nitrogen dioxide gas and carbon dioxide. The nitrogen dioxide forms a layer on top of the ensilaged fodder. Above this layer, which may be of variable

depth, is normal air. Thus an individual preparing to enter the silo from above encounters breathable air and may be misled into believing that the atmosphere within the silo is safe. Only after dropping down to the top of the fodder does he encounter the oxygen-depleted air and nitrogen dioxide. Illness in which the symptoms do not manifest themselves for several hours may follow inhalation of sub-lethal concentrations of nitrogen dioxide.

The knowledge to prevent silo deaths exists and if it is applied, accidents should not occur. That they continue to occur year after year is an indication that the preventive measures applied in day to day farming are ineffective.

Pladson (1984) reported that farmers may develop three different illnesses from entering their silos. He described three case reports of individuals developing one of the three disease entities. The cases emphasize the differences and similarities of the three diseases: silo filler's disease, farmer's lung disease, and pulmonary mycotoxicosis. The history is the most important tool to assist diagnosis. Because of the difference in prognosis and treatment of these disorders, it is important to differentiate these diseases.

Liesivuori and Kettunen (1983) studied farmers' formic acid exposure by field measurements in the silage-making season at 14 Finnish farms. Two preservative solutions were used which differed in concentration of formic acid. Time-weighted average exposure to the acid vapour varied with the tasks carried out in the open air from 0 to 30 mg $m^{3}$, while vertical silo filling caused an exposure of from 0 to 7.0 mg $m^{3}$. Comparable figures were found for the horizontal silos, while adding the formic acid on the surface of forage in the silo caused exposures ranging from 33 to 99 mg $m^{3}$. These latter concentrations were considered to constitute a significant health hazard especially in farmers with cardiovascular diseases; formic acid is an inhibitor of mitochondrial cytochrome oxidase thereby inducing histotoxic hypoxia. Goggles and respirators should be used in the silos to prevent acid spills and inhalation of acid vapour.

Schrottmaier (1982) reported that in Austria each year five to ten people die because of fermentation gases in silos. This is why the BVPA-Wieselburg was instructed by the Ministry of Agriculture and Forestry to research into safety equipment for silos to reduce accidents. Measurements of the composition and concentration of gases during the filling or opening of more than 70 different silos were made. Also, simulation experiments were performed to gain knowledge of the influence of the cover or hatch position, the contents of the silo and the outside wind conditions on the out-flow of the gases. The effects of technical devices such as blowers, flaps, etc. to prevent accidents were studied and encouraging results were found.

Horvath et al (1978) reported on twenty-three patients exposed to nitrogen dioxide in agriculture or industry who were referred to the University of Wisconsin Medical Center. Eighteen experienced a transient upper respiratory tract syndrome; five developed pulmonary edema or bronchiolitis obliterans. This latter group responded to steroid therapy but all demonstrated evidence of persistent pulmonary dysfunction on follow-up studies.

Combining their findings with those in the literature they concluded : (1) exposure to $NO_2$ is more common than generally appreciated; (2) case fatality is high - 29% for silo-filler's disease; (3) steroids are effective therapy and should be continued for at least eight weeks; (4) although the majority recover without significant sequelae, some individuals may develop persistent functional abnormalities; (5) there is no evidence that long-term exposure to low concentrations of $NO_2$ leads to chronic airway obstruction; and (6), $NO_2$-induced pulmonary disease could be eliminated with appropriate preventive measures.

Fleetham et al (1978) reported two incidents of silo-filler's disease.

Incident I : In mid-September 1977 three previously healthy men aged 31, 33 and 47 years after entering a silo that had been filled with corn the previous day.

Incident II : A 27-year-old nonsmoking farmer was admitted to hospital with progressive dyspnea. Two months previously he had felt nauseated and short of breath for 24 hours after entering a recently filled silo. Although he felt well for the next 2 to 3 weeks, he subsequently became short of breath to the extent that he was unable to work.

Three years later the man was asymptomatic and his chest roentgenogram was normal, but pulmonary function tests revealed a persistent mild obstructive defect and reduced diffusion capacity.

Morrissey et al (1975) reported the effects of oxides of nitrogen inhalation in a 21-year-old gardener exposed to silage gas. Initial nausea, cough and fever remitted, but respiratory failure developed 3 weeks later. Roentgenograms and lung function studies revealed pulmonary edema, volume restriction, and severely impaired gas exchange. Needle biopsy showed a nonspecific interstitial pneumonia. With steroid therapy all functional parameters except diffusing capacity returned to normal. Failure to inquire about non-occupational activities led to delayed diagnosis.

Scott and Hunt (1973) described four episodes of silo filler's disease in three patients with serial pulmonary function studies. Obstructive, restrictive and diffusion defects were observed acutely, with almost complete clearing of detectable disease within the observation period (327, 10, 75 and 28 days). An analysis of the information concerning chronic pulmonary disease and nitrogen dioxide exposure leads the authors to conclude: 1) silo filler's disease may occasionally lead to chronic pulmonary disease by (a) the survival of the patient, despite severe bronchiolar injury by the nitrogen dioxide or more commonly, (b) less severe residual bronchiolar injury after exposure in patients with pre-existing 'small airway disease' (chronic bronchitis and emphysema predominantly): 2) animal exposure studies and lung biopsies in human beings lead to the speculation that the chronic disease which is produced may be centrilobar emphysema.

Ramirez and Dowell (1971) followed a patient for 7 years after exposure to silage gas. His chest film showed diffuse reticular and fine nodular infiltrates. Except for mild hypoventilation and hypoxemia his pulmonary function has remained normal. Persistent lung malfunction after exposure to silage gas is uncommon in those patients who recover from the initial toxic pulmonary edema. Reported cases of chronic lung disability after silage gas inhalation were probably due to other causes, such as chronic bronchitis.

Kavoussi (1974) reported on a study begun in June 1970 at which time the silo had been in operation for 33 years. The labor turnover for this period had been very low and this provided an excellent opportunity for examining the possible relationship between the development of pneumoconioses and various factors associated with the work at the silo. The principal factor requiring investigation was the duration of exposure to the dust and its relationship with the incidence of pneumoconioses.

Lowry and Schuman (1956) reported on four patients who entered silos within a day or two after filling with corn silage and noted irritating fumes and experienced respiratory symptoms of varying degrees of severity. A period of failure to improve was followed by a period of worsening that ended with death on the 27th and 30th days in two cases. The disease was halted in the other two cases by treatment with prednisone. Intramuscular injections of this drug in 10mg doses three times daily were followed by prompt and striking improvement, especially in one case. Chemical evidence showed that the toxic gas was probably nitrogen dioxide, a gas capable of causing early pulmonary edema with subsequent bronchiolitis fibrosa obliterans. The bronchiolitis gives a roentgenogram marked by innumerable discrete nodular densities in the lungs and indistinguishable from that of acute miliary tuberculosis; its nature was verified at autopsy in the two fatal cases. Oxygen gave only symptomatic improvement, and the effects of bronchodilators and antibiotics were only temporary. Prevention of silo-filler's disease depends

on adequate ventilation, on means of keeping people and animals from straying into dangerous spaces adjoining a silo, espcially during the 7 to 10 days after the silo is filled, and on a wider recognition of the danger.

In August 1954 Grayson (1956) encountered two cases of acute respiratory disease due to inhalation of silage gas. One was fatal. A thorough investigation of these two cases of the silage gas that caused the illness indicates that the disease was caused by the oxides of nitrogen. The two cases, therefore, are believed to the first cases reported in the literature of poisoning from silage gas in which it was definitely proved that the noxious agents were the oxides of nitrogen.

## Grain Handler's Disease

Broder et al (1984) studied the health effects of employment as a grain handler by examining workers on two occasions, firstly, immediately before or soon after they were hired and again about two and a half months after they were employed. Over this time there was a substantial increase in the prevalence of cough, sputum, and eye irritation, accompanied by small pulmonary function changes suggestive of a restrictive ventilatory defect. No comparable changes in symptoms were observed over a similar number of months in grain handlers employed for an average of nine years or in control workers consisting of newly hired or long term civic outside labourers. The long term grain handlers, however, developed a similar change in their pulmonary function. These findings indicate the occurrence of a change in the health of grain elevator workers after a relatively brief duration of employment.

In order to study the effects of grain dust exposure DoPico et al (1984), compared respiratory parameters between 310 grain handlers and 237 city workers of comparable age, height, weight, and smoking habits. Both populations resided and worked in the same geographic area of the United States. Information was obtained by questionnaire, interview, and examination. Pulmonary

function tests included $FEV_1$, $FEF_{25-75}$, $Vmax_{50}$, $Vmax_{75}$, CV, ©N2/L, and $DL_{CO}$. The prevalence of acute work-related and chronic respiratory symptoms of auscultatory bronchi, and of airways obstruction ($FEV_1/FVC<0.7$) were significantly higher ($p<0.05$) in grain handlers than in control subjects. The mean values of all lung functions except CV, © $N_2/L$, and $DL_{CO}$ were significantly lower in grain workers than in control subjects. The effects of smoking and grain handling on symptom prevalence and lung functions adjusted for age and height, analyzed by logistic regression model, were highly significant (p values ranged from 0.00001 to 0.5) and independent. The odds of having chronic bronchitis or wheezing at work were, respectively, increased 4.4-fold and 4.8-fold by grain handling and by 2.9 fold and 1.9-fold by smoking. Grain handling increased the odds of having airways obstruction 2.6-fold and smoking increased it 2.7-fold. It was concluded that grain handlers have a higher prevalence of chronic bronchitis and other respiratory symptoms than do comparable workers who do not handle grain. The effect of grain dust exposure on symptom prevalence is usually greater than that of smoking. Grain handling has an adverse effect on lung function that is of the same or smaller magnitude than that of smoking. The effects of smoking and grain handling were additive but not synergistic.

Stepner et al (1984) did a study to attempt to develop an animal model of grain workers' lung. The development of such a model would enable them to determine whether changes are observed which might provide a basis for obtaining further insight into the nature of the human condition.

Skea and Broder (1984) described studies which show that the presence of phenol in grain dust extract leads to the formation of what appears to be a tannin-like material which accounts for the IgG precipitating activity and much complement fixing activity. However, there is a smaller amount of endogenous material present in grain dust extract lacking phenol which possesses similar properties.

Broder et al (1983) examined possible mechanisms of the obstructive and restrictive ventilatory defects of grain elevator workers. They found that grain handlers whose skin tests were positive to grain of fungal antigens had no excess of respiratory symptoms or pulmonary function abnormalities. Also, those having a possible work-related respiratory showed no response to inhalation challenge tests with grain dust extract. In addition, grain handlers exhibited neither an increase in positive serum precipitin tests with fungal antigens nor abnormal serum levels of C3 and C4, C-reactive protein, rheumatoid factor or antinuclear factor. However, their serum al-antitrypsin level was elevated. The latter finding may be indicative of a pulmonary inflammatory process, but they found no clear indication of a type 1 or 3 allergic state in grain elevator workers.

Cotton et al (1983) measured in four groups of individually-matched subjects (non-smoking grain workers, smoking grain workers, non-smoking controls and smoking community controls) measured pulmonary function variables from the spirogram, from the maximal expiratory flow-volume curve breathing air and helium and from the single breath nitrogen test as well as symptom prevalences from a questionnaire in order to assess the relative effects of smoking and occupational exposure to grain dust in Saskatchewan country grain elevators. There were similar increased prevalences of respiratory symptoms and reductions in pulmonary function associated with either grain dust exposure or smoking, but the effects of smoking were slightly more pronounced. The combined effects of grain dust and smoking on lung function appeared to be additive except in the least exposed workers (five years or less) where a synergistic effect was observed in tests of peripheral airways dysfunction.

Warren and Manfreda (1983) performed a study to determine whether grain farmers developed chronic bronchitis, airflow obstruction, grain fever and acute dyspnea on exposure to grain. A study population of both sexes, aged 20 - 65 years, in two rural municipalities was compiled from the Provincial Population Registry cross-checked with electoral rolls. 1902 subjects, 82%

of those eligible took part in the study which was carried out in winter and spring of 1978 and 1979. The subject's respiratory symptoms, disease, smoking habits, involvement with farming and place of residence were recorded by a questioner. One half of the males were current farmers; one quarter had never farmed. 77% had grown grain the survey year; 93% had in the past 10 years. Exposure to grain was estimated from the number of days spent handling grain. 43% of farmers and 33% of nonfarmers had never smoked. Farmers and nonfarmers had a similar frequency of sensitization of allergens and similar IgE levels. From this study, it was concluded that some chronic respiratory symptoms are associated with farming in non-smokers, but the researchers could not be sure that this was due to grain exposure. It was found that lung function is worse in farmers than nonfarmers, particularly those with symptoms. Dyspnea with exposure to grain was common and was associated with sensitization to allergens and decreased lung function. Grain fever was associated with exposure to mouldy grain, was commoner in non-smokers and was not related to sensitization to allergens or decreased lung function.

Grain farmers and nonfarmers from a rural community, were compared by Manfreda et al (1982) for a determination of whether grain farming is associated with an increased risk of developing respiratory symptoms, diseases, and chronic airflow obstruction detected by spirometry. In addition the role of factors such as smoking atopy defined by allergy esting, total immunoglobulin E (IgE) in serum, and blood eosinophils was also assessed. Information on symptoms, diseases, smoking, and occupational and residential history was obtained by a questionnaire. The subjects studied (1,902 in number) represented 83% of the eligible population in the community, were 20-65 years of age, and were evenly divided between the sexes. About half were grain farmers. About 43% of the males and 72% of the females had never smoked; these proportions were higher for the farmers than for the nonfarmers. Allergic reactions to house dust (22%) were the most common, followed by mites (19%), moulds (15%), grasses, trees and weeds (9%) and Aspergillus. Penicillium and grain dust (8%); there was no significant difference between the farmers and

nonfarmers. Shortness of breath on exposure to grain dust developed in one-fifth of the farmers and was associated with atopy. History of grain fever (reported by 13% of the farmers) was significantly more common for the nonsmokers and for those who had been exposed to mouldy grain. There was an excess (10%) of chronic bronchitis and wheezing in nonsmoking male farmers, but this excess was not related to the intensity of grain exposure. Lung function was determined by smoking, atopy, and IgE. It was worse in male farmers than in nonfarmers, particularly if they had symptoms. Results of the study show that respiratory disorders are more common in farmers than in nonfarmers. While acute respiratory symptoms (shortness of breath and grain fever) are clearly related to grain exposure, such a relationship is less convincing for chronic bronchitis and chronic airflow obstruction. In addition to exposure to environmental irritants and smoking, individual susceptibiliity such as atopy should be considered in prevention programs for respiratory disorders in farmers.

Johlonen et al (1982) reported a study that was based on data provided by 12,056 Finnish farmers. The data were gathered by a postal survey conducted by the Social Insurance Institution of Finland. Some parts of the data were collected by clinical examinations and laboratory tests of immunology in seven health centres and the Kuopio University Hospital. According to the survey the prevalence of asthma was 2.7% among the farmers. The prevalences of chronic bronchitis and farmer's lung were, respectively, 6.5 and 1.6%. Asthma and chronic bronchitis were twice as common among smokers than non-smokers, whereas the reverse was true for farmer's lung. Asthma, chronic bronchitis, and farmer's lung occurred more frequently among atopic than nonatopic farmers. There were also significant differences in the prevalences of each disease between the various types of farm production. Precipitating antibodies against Aspergillus fumigatus, Aspergillus umbrosus, Micropolyspora faeni, or Thermoactinomyces vulgaris were found in 11.6% of the 2,470 farmers examined in the health centers. Most frequently antibodies were formed against Aspergillus umbrosus, in 4.8% of the farmers. The respective findings for Aspergillus fumigatus,

Thermoactinomyces vulgaris and Micropolyspora faeni were 1.6, 3.9 and 1.3%. The prevalences and relative frequencies of the four types of antigens closely correlate with the findings of previous smaller studies done in Finland, Great Britain, the United States and Canada.

Cotton et al (1982) studied two groups of young male cereal grain elevator workers: 82 lifetime non-smoking grain workers (2.5 +-1.2yr of dust exposure) who were 22.7 +- 3.5 yr of age, and 82 smoking grain workers (6.1 +- 4.1 pack-years of smoking) individually matched to the non-smoking grain workers for age (22.7 +- 3.3 yr) and years of work in the grain industry (2.6 +- 1.3yr). They also studied the following groups of community control subjects: 82 non-smoking community control subjects individually matched to the non-smoking grain workers for age (22.8 +- 3.7 yr), and 82 smoking community control subjects individually matched to the smoking grain workers for age (22.7 +- 3.6yr) and smoking history (6.0 +-4.0 pack-years). They measured forced expiratory volume in one second ($FEV_1$), forced vital capacity (FVC), $FEV_1$/FVC%, the maximal mid-expiratory flow rate ($FEF_{25-75}$) the flow at 50% ($Vmax_{50}$) and 25% ($Vmax_{25}$) of a maximal expiratory flow-volume maneuver, the percent increase in the maximal expiratory flow at 50% FVC breathing a mixture of 80% helium-20% oxygen as compared with air (©$Vmax_{50}$) and the slope of Phase III of the single breath nitrogen test (©N2/L). They also assessed the prevalence of respiratory symptoms from responses to a standardized questionnaire. Smoking was associated with an increased prevalence of cough, wheezing, and dyspnea, and a mildly decreased $FEV_1$/FVC%. Two variables were used as indexes of small airway dysfunction, a lower ©$Vmax_{50}$ and a higher ©$N_2$/L. Only the group of workers who both smoked and were occupationally exposed to grain dust had evidence of small airway dysfunction. The differences in ©$N_2$/L and ©$Vmax_{50}$ were greater than was expected from an additive model, suggesting that the combined effects of occupational exposure to grain dust and inhalation of cigarette smoke may have a synergistic effect leading to small airway dysfunction in young cereal grain workers.

Peters et al (1982) described the clinical and neuropsychiatric features of seven workers from the grain storage industry. All were exposed to fumigants, especially carbon disulfide and malathion. Clinical manifestations included cogwheel rigidity, resting and action tremor, peripheral neuropathy, pyramidal tract signs, an EEG pattern of sleep apnea, and characteristic measurable neurobehavioral dysfunction. Similar signs and symptoms due to carbon disulphide exposure in the viscose rayon industry strongly supported the conclusion that these grain storage workers were suffering from carbon disulfide poisoning. Malathion exposure probably had a contributing role. They concluded that exposure to these fumigants poses a serious occupational risk to the nervous system.

Corey et al (1982) attempted to determine whether grain handlers underwent work-related changes in their pulmonary function and, if so, to examine the dose-effect relationships with dust exposure. The pulmonary function of grain handlers was measured at the beginning and end of work shifts over a period of one week, during which their exposure to dust was measured daily. The results showed changes indicative of a within-day obstructive change, in addition to a small restrictive defect occurring over the course of a week. Civic outside labourers who were examined as a control group showed a similar within-week obstructive change without any associated restriction of lung volume. The data on the grain handlers were also used to examine the dose-effect relationships of dust exposure, both on baseline pulmonary function and on within-day changes in these measurements. The baseline flow rates of workers who did not wear a mask were found to vary inversely with their average exposure to respirable dust. In addition, the flow rates underwent a within-day decrease that varied directly with their corresponding exposure to respirable dust and was unrelated to mask wearing. The median of the slopes for this relationship indicated that 50% of the subjects had a decrease of at least 923ml/s in the value of their Vmax50%VC for each $1mg/m^3$ increase in the concentration of respirable dust. Non-respirable dust did not have a measurable effect either on the baseline or the within-day changes in pulmonary function. The acute changes were unaffected by age, duration of employment,

or extent of smoking.

Herbert et al (1981) studied grain handlers employed at three large inland grain terminals along with an equal number of office workers matched for sex, age and smoking history. Respiratory symptoms and spirometric abnormalities were no more frequent in 16 grain handlers who were non-smokers than in their controls. However, 20 grain handlers who were smokers complained significantly more ($P < 0.01$) of grade 1 dyspnea and had significantly lower ratios of forced expiratory volume in the first second to forced vital capacity ($P < 0.05$) than their controls. Only 3% of the grain handlers were sensitive to grain dust, and 18% were found to be atopic but to have good lung function. A family history of asthma or allergic rhinitis was no more frequent in the grain handlers than in the control subjects. It was concluded that the combination of cigarette smoking and exposure to grain dust causes a deterioration in lung function.

DoPico et al (1981) reported on the results of their cross-sectional epidemiologic study to determine the relative importance of the effects of cigarette smoking and grain handling on symptom prevalence and lung function, and of a study undertaken to identify the constituent of grain dust responsible for grain handlers' respiratory symptoms and the potential pathogenic role of mediator release and complement activation.

Patel et al (1981) undertook a pulmonary survey in a large granary in the West of Scotland. The lung functions and respiratory symptoms were compared in nineteen atopic and fifty-six non-atopic grain handlers with reference to their smoking habits and also to forty-eight control subjects with no previous exposure to grain dust. Cigarette smokers from the granary workers and the control group had more respiratory symptoms and significantly lower PF, $FEV_1$, $V_{25}$ and $V_{50}$. The atopic grain handlers, on the other hand, had better ventilatory functions compared to non-atopic workers. This difference in the atopic group may be related to their lower cigarette consumption, shorter service in the granary or the process of self selection.

The grain handlers with wheeze or breathlessness at work had significantly higher incidence of restrictive type MEFV curves and this could not be attributed to increased cigarette consumption, atopy or longer duration of employment and there was no correlation between severity of symptoms and occupational exposure. Although PF< $FEV_1$, FVC, $V_{25}$, $V_{50}$ and $V_{75}$ failed to show significant differences in granary workers and controls, the shape of MEFV curve may have significance as a sensitive indicator of the effect of grain dust as a preclinical stage.

In an important Canadian study Chan-Yeung et al (1981) conducted a respiratory survey on 587 grain elevator workers in the Port of Vancouver and on 111 civic workers, 2.5 years after a first health survey. The prevalence of respiratory symptoms and lung function findings among grain elevator workers in the second survey were almost identical with those in the first health survey, even though the dust concentration was lower in the elevators during the second survey. The longitudinal study in 396 grain workers showed that the prevalence of respiratory symptoms increased slightly during the second health survey among workers who had the same smoking habits during both surveys. Of the smokers who had respiratory symptoms or lung function impairment in the first survey, 23.5% followed our advice and gave up smoking; the prevalence of cough and sputum production decreased among these workers. The annual decline in function was greater for grain workers than civic workers particularly among workers over the age of 50 years when the differences in annual decline in forced expiratory volume in 1 sec ($FEV_1$) and maximal mid-expiratory flow rate (MMF) between the two work groups became statistically significant. The annual decline in lung function was significantly correlated with age and smoking for both work groups. Cigarette smokers had a greater decline in lung function than non-smokers, and older workers also showed a more rapid decline in lung function compared to younger workers. The relationship between $FEV_1$, FVC, and MMF with age was quadratic rather than linear. Among grain workers the decline in lung function was not correlated with initial lung function, presence of respiratory symptoms, atopic status, or duration of exposure. It was, however, correlated with the acute changes in

lung function over the course of one work shift and one work week. The conclusion was that grain dust has deleterious effects on the lung function of the workers and that it should not be regarded as a nuisance dust.

Grzybowski and Chan-Yeung (1980) studied the influence of atopy on the prevalence of respiratory symptoms and lung function abnormalities in 569 workers exposed to grain dust. There was no significant difference in the prevalence of respiratory symptoms between atopic and nonatopic workers. The prevalence of atopy was compared in different occupational groups.

Warren and Manfreda (1980) reported that of a random sample of farmers in two crop districts of Manitoba mailed a respiratory questionnaire in 1976, 833 (82% of those currently farming in the area) replied. More than half were grain farmers and nearly half had never smoked cigarettes. The prevalence of chronic cough and phlegm production, wheezing and exertional dyspnea was positively related to the amount of smoking but was also higher than expected in non-smokers. Acute dyspnea, sometimes of delayed onset accompanied by fever, was most commonly related to handling old grain and was reported by 44% of the farmers. Current smokers were more susceptible than non-smokers to this type of dyspnea. Farmers with a history of acute dyspnea while handling grain were more likely to wear masks, but the overall rate of mask wearing, even among those at highest risk, was low.

Broder et al (1980) examined a group of 77 grain elevators at monthly intervals over a 7-month period. Approximately half of the workers were temporarily laid off for several months of this period, during which those who were steadily employed were involved in processing a reduced throughput of grain. The men who were laid off showed a transient decrease in some respiratory symptoms during the months of layoff, followed by an increase after rehire. Those who were steadily employed showed a corresponding increase in these symptoms during the period of reduced grain movement, which did not change when the elevator returned to full activity. All of them demonstrated the greatest

maximal expiratory flow rates during the midportion of the period of reduced work status, and the lowest values after either rehire or the restoration of full elevator activity. These longitudinal changes in respiratory variables are largely consistent with the effects of grain dust exposure, which may be at least partially reversible.

Dosman et al (1980) in order to determine whether clinical symptoms and pulmonary function abnormalities were more common in lifetime non-smoking grain elevator workers exposed to grain dust than in lifetime non-smoking community control subjects who were not occupationally exposed to dust, obtained an occupational health questionnaire, spirometric variables, and flow-volume curves on 90 lifetime non-smoking grain workers and 90 lifetime non-smoking community control subjects. For these groups the prevalence of chronic bronchitis, defined as daily production of phlegm for 3 months/yr for at least 2 years. The prevalence of chronic bronchitis was higher in non-smoking workers (23.1%) than in non-smoking control subjects (3.3%)($p<0.01$). Non-smoking grain workers had lower mean values than did non-smoking control subjects for maximal mid-expiratory flow rate ($p<0.01$) and for maximal expiratory flow at 50% of vital capacity ($p<0.01$). They concluded that exposure to grain dust in lifetime non-smoking grain workers is associated with an increased prevalence of chronic bronchitis and evidence of airflow construction.

Mink et al (1980) measured nonspecific bronchial reactivity to inhaled histamine in 29 lifetime nonsmoking grain handlers and 29 lifetime nonsmoking unexposed control subjects matched for age, sex and specific conductance. Routine lung function tests revealed a total lung capacity that was higher in control subjects than in workers ($P<0.05$) with no difference in other subdivisions of lung volume, or expiratory flow rates between the two groups. An index of allergy was significantly greater in the control subjects than in the grain workers ($P<0.01$). None of the grain handlers was sensitive to grain dust by history or by skin tests. Respiratory symptoms (cough, sputum, dyspnea, or wheezing) were more prevalent in the grain workers than in controls ($P<0.05$). The mean concentration of histamine required

to reduce the specific conductance by 35 percent was 4.5+-2.0mg/ml in grain workers and 5.9+-3.0mg/ml in controls (P<0.05)> Chronic exposure to grain dust in nonallergic individuals appears to be associated with both increased prevalence of respiratory symptoms and increased nonspecific bronchial reactivity when compared to nonexposed control subjects.

Chan-Yeung et al (1980) carried out epidemiologic health surveys among 610 workers in the 5 grain elevators in British Columbia and 2 control groups consisting of 136 civic workers and 187 non-cedar sawmill workers. A medical and occupational questionnaire was administered by trained interviewers. Spirometry was performed on site using a 13.5 Collins spirometer. Skin tests were performed using various antigens, and serum samples were obtained for determination of a-antitrypsin concentration and phenotype, and precipitin studies. Dust concentration was measured by both personal area sampling methods in the grain elevators and sawmills. There was a higher prevalence of eye, nasal, and chest symptoms (cough, sputum, wheeze, and breathlessness) among grain workers than among control subjects. The mean values for spirometric indices of pulmonary function ($FEV_1$ and FVC) were slightly lower among grain workers than control subjects. The estimated decreases in $FEV_1$, FVC and FEF during the middle half of the FVC with age were also greater for grain workers than for control subjects. The mean pulmonary function test results improved during the work week among sawmill workers, but decreased during the work week among grain workers, suggesting that grain dust has acute deleterious effects on pulmonary function in some workers. Regardless of the work group, current smokers had more chest symptoms and lower pulmonary function test results than ex-smokers and nonsmokers. No potentiating effect of smoking and exposure to grain was demonstrated. There was no correlation between the duration of the employment in the grain elevator and deterioration of respiratory function.

Broder et al (1980) presented a report on one part of the results obtained in a study of respiratory parameters in grain

handlers and civic outside workers in Thunder Bay. A persistent cough was reported in a 20% higher frequency among grain handlers than civic outside workers matched for smoking and in a 45% higher frequency among smokers than nonsmokers within occupational groups. A similar trend was seen in other lower respiratory symptoms. The effect of grain and smoking on cough was additive. Among grain handlers the FVC and $FEV_1$ were slightly lower than in civic workers and in smokers the $V_{25}VC$ and $DL_{CO}$ were lower than in nonsmokers. The effect of grain was appreciable but was exceeded by the effect of smoking.

Respiratory variables were compared by Broder et al in 441 grain elevator workers and 180 civic outside labourers in Thunder Bay. The grain handlers had a lower frequency of both positive skin reactions to pollens and moulds and a family history of asthma, which suggests that they may have been self-selected for a decreased tendency to develop allergic respiratory disease. There was a higher frequency of cough and rales and a small decrease in FVC and $FEV_1$ among the grain handlers, as compared to the civic workers matched for smoking. However, these differences between grain and nongrain workers were small in comparison to those between smokers and nonsmokers. There was no clear indication of a worsening of respiratory functions that could be attributed specifically to duration of employment as a grain elevator worker.

Chan-Yeung et al (1979) studied 22 grain workers with respiratory symptoms and lung function abnormalities. Our findings suggest that grain dust asthma probably has an allergic basis, even though skin tests and precipitin studies were negative using extracts of grain dust. Hypersensitivity pneumonitis and grain dust fever were not found in any of the subjects. They found that grain dust can cause air-flow obstruction in two ways: first by inducing asthma, probably through immunologic mechanisms, and second, by causing industrial chronic bronchitis.

Gerrard et al (1979) carried out a study to determine whether respiratory disease in Saskatchewan grainhandlers was or was not

due to hypersensitivity to grain dust. Sixty nonsmoking grainhandlers, half of whom had low $FEV_1/FVC$ ratios and half of whom had high, were studied. The findings in grain-handlers were compared with those in 30 age-matched, nonsmoking teachers. In the group of grainhandlers with low $FEV_1/FVC$ ratios, one had developed asthma associated with exposure to grain dust. The majority were healthy, had $FEV_1/FVC$ ratios of 70% or greater, and had less evidence of allergic respiratory disease than had age-matched teachers. The studies suggest that non-atopic, nonsmoking men can work in grain elevators without developing respiratory disability, though they may develop a small but significant increase in nonspecific bronchial reactivity to histamine.

Dosman et al (1979) commented on chronic bronchitis and exposure to cereal grain dust, particularly with workmen involved in the grain storage and transporting industry. Populations at risk in these industries include approximately 500,000 workers in the US and 30,000 workers in Canada. These numbers include elevator agents, workmen in large terminals, dock workers, bakers, and mill workers whose work areas are situated within or adjacent to facilities involved in the bulk movement or processing of various cereal grain products. Grain dust is a heterogeneous substance than includes organic substances from various cereal grains (wheat, barley, rye, oats, and corn) as well as contaminants including silica, fungi and their metabolites, bacterial endotoxins, insects, mites, mammalian debris, and various chemical substances used as herbicides and pesticides in both growing and transporting activities. In Canada, a recently inaugurated health surveillance program includes regulations aimed at decreasing threshold limit values of airborne grain dust to which an employee is exposed to 10mg/m3 averaged during and 8-hour day and a 40-hour week using a time-weighted average with dust collections made when the facility is functioning at least at 70% of its rated capacity. Although it is not known what effect decreases in dust concentration mught have on pulmonary function test variables, a decrease in atmospheric pollution is likely to result in a decrease in the

prevalence of chronic bronchitis in these workers. The available data also suggest that a significant decrease in chronic sputum production might be achieved if the workers were able to alter their smoking habits.

Cotton and Dosman (1977), at the International Symposium on the Effects of Grain Dust on Human Health held at the University of Saskatchewan, 7-9 November 1977, reported on the environmental factors in grain dust and health. Control of dust levels inside grain storage facilities is necessary both to reduce the risk of respiratory damage to the workers and to eliminate serious explosion hazards. Dust control generally consists of supplying shrouding devices or hoods at all points where grain is unloaded or reloaded. From such hoods, dust is aspirated by means of fans to bag filters or cyclones. However, in many areas of Canada and the USA, the dust (in quantities averaging 1.26906kg per 1.016 metric ton [2.8lb per ton] of grain) is not taken to a separate bin for disposal but is eventually returned to the grain stream and is recirculated to the system. The following points were agreed upon :

1. Levels of crude grain dust are high in many grain storage and transporting facilities

2. A threshold limit value of $10mg/m^3$ appears to be a reasonable goal to achieve, based on existing knowledge

3. The technology exists to reduce dust levels to $10mg/m^3$ but the economic feasibility has not been ascertained.

4. Continued research is necessary to characterize the constituents of grain dust and their possible relation to health

Cotton and Dosman (1977), at the International Symposium on the Effects of Grain Dust on Human Health, University of Saskatchewan, 7-9 November 1977, commented on host factors in grain dust and health. They believed that the primary focus of research should be on characterizing the diseases induced and their relations to the agents to which workers are exposed. This requires combined epidemiologic and environmental studies. Such studies are complicated by the dispersed locations of the

facilities, the seasonal aspects of the industry, and the climatic conditions. Additional research must also be carried out into the role and mechanism of action of the components of grain dust. This should include consideration of the toxic effects of agricultural pesticides and chemicals. These studies require collaborative approaches between the basic laboratory sciences, clinical medicine, and other disciplines including toxicology, immunology, mycology, physiology, and chest medicine. The interactions and synergisms that may take place between the components involved in grain dust exposure and host factors must be identified. The relation between acute exposure and subsequent dysfunction should be investigated.

Farant and Moore (1978) surveyed conditons at eight terminals, nine transfer and fourteen country grain elevators. The exposure data obtained from the survey results are based on the assumption that work practices for a specific job category, at a common worksite, are similar in all the elevators studied. On this basis, mean exposures have been calculated for specific job titles and worksites and related to the status of dust control measures in effect and the degree of grain handling activity.

DoPico et al (1977) reported on a survey of 300 grain elevator workers which revealed that 77% complained of eye symptoms; 64% of nasal symptoms; and 88% of one or more respiratory symptoms on exposure to airborne grain dust. Symptoms on exposure were independent of age and length of employment. Cough and wheezing on exposure were more common among smokers than nonsmokers ($P<0.025$). Nineteen percent of the workers had had episodes of grain fever. The prevalence of chronic bronchitis was 37% (42% of smokers and 30% of nonsmokers). Wheezes on auscultation were found in 23%. Measurements of lung ventilatory function, as well as diffusing capacity, correlated significantly with age and smoking habits, but not with length of employment. Thirty-seven percent of the workers had an abnormal mean forced expiratory flow during the middle half of the forced vital capacity (40% of smokers and 13% of nonsmokers), whereas only 13% had an abnormal ratio of 1-sec forced expiratory volume to forced vital capacity.

There was no correlation between precipitins to fungi, bacteria, grain, or grain dust antigens and acute or chronic respiratory symptoms, lung function, or grain fever. There was, however, a significant correlation between cutaneous reactivity to grain dust and wheezing on exposure ($P<0.02$). Abnormal flows at low lung volumes were more common among cutaneous reactors to common allergens. They concluded that exposure to airborne grain dust could cause acute inflammatory reaction to the exposed mucosa, and it is highly probable that grain dust contributes, and in some cases, causes chronic airway disease.

NIOSH (1976) conducted a Health Hazard Evaluation Determination at Cargill Elevator - Terminal 4, Portland, Oregon in July 1976 and found at the time of the evaluation, no serious health hazard was believed to exist at the Cargill Grain Elevator - Terminal 4.

Darke et al (1976) surveyed the incidence of respiratory symptoms caused by grain dust during harvesting in a group of Lincolnshire farmers. A quarter complained of respiratory distress after working on combine harvesters or near grain driers and elevators, with cough, wheezing, and breathlessness, sometimes so severe as to prevent work. The airborne dust around combine harvesters contained up to 200 million fungus spores/$m^3$ air with Cladosporium predominant while drivers were exposed to up to 20 million spores/$m^3$ air. Verticillium/Paecilomyces type spores, mostly from Verticillium lecanii, Aphanocladium album, and Paecilomyces bacillosporus, were abundant in the dust. Extracts of these species produced immediate weal reactions in skin tests, precipitin reactions with sera, and rapid decreases in $FEV_1$ when inhaled by affected workers. There were no delayed reactions. Results suggested type 1 immediate hypersensitivity to the spores although the physical effect of a heavy dust diposit could be important. Drivers could be protected by cabs ventilated with filtered air.

Davies et al (1976) performed bronchial provocation tests on two separate occasions in a farmer with dust from his own grain; this led to immediate and late respiratory reactions

followed, without further exposure to grain dust, by severe respiratory problems during subsequent nights. Studies of lung function, including measurements of closing volume, suggested that both large and small airways rather than lung parenchyma were primarily involved. Examination of the grain samples together with the results of skin and serologic tests suggested that the grain mite, Glycphagus destructor, might be an important allergen. Serum concentrations of C3 and C4 did not alter during these recurrent nocturnal asthmatic reactions.

Kleinfeld (1974) compared the prevalence of respiratory symptoms and pulmonary ventilatory impairments of grain handlers and bakers. The grain handlers were exposed to crude grain whereas the bakers were exposed to a milled grain. The study included 55 grain scoopers engaged in the removal and transfer of grain such as wheat, oats, barley, corn and soybeans from the holds of ships to grain elevators for storage. A similar study was conducted on a matched group of bakers employed at making bread, cakes and other baked specialties requiring the use of flour and other ingredients.

Comparative clinical and pulmonary function findings among grain handlers and bakers, whose mean age and mean dust exposure were essentially similar showed that each occupational group had a relatively high prevalence of respiratory symptoms and dermatitis. Of the pulmonary ventilatory function findings, the grain handlers showed a lowered mean $FEV_1$ compared to the bakers.

Tse et al (1973) reported that a survey of 68 grain elevator agents in Southern Manitoba disclosed that 75% had respiratory symptoms. Chronic cough and sputum, and dyspnea associated with exposure to grain dust were common. These symptoms were reported in more than half of the smokers and ex-smokers and in more than one quarter of the nonsmokers. Twenty-seven percent of the subjects also developed systemic symptoms of 'grain fever' after exposure to grain dust. Lung function tests demonstrated abnormal spirometric results in 37%, while estimation of the 'closing volume' demonstrated abnormality in 42.5% of the subjects, even after the values have been standardized for

smoking habit. The high prevalence of respiratory symptoms and abnormal lung function among these subjects indicated that exposure to grain dust was an important etiologic factor in their development. Hypersensitivity to grain dust was found in eight subjects by prick skin testing and in six subjects by precipitin test. There was no significant correlation between the presence of positive skin or precipitin test and clinical disease.

Warren et al (1973) performed allergic and respiratory investigations in 17 subjects with respiratory symptoms and occupational exposure to grain dust. Common symptoms included chronic cough and sputum productiuon, grain fever, wheezing and dyspnea on exposure to grain dust. Results of pulmonary function tests demonstrated a pattern of obstructive airway disease. Immediate hypersensitivity to grain dust was common. Both immediate and late reactions were observed on inhalation challenge studies. There was a good correlation between the hypersensitivity reactions on skin testing and on bronchial provocation. Inhalation of crude grain dust extract may produce systemic symptoms of malaise, myalgia, headache, and leukocytosis even in normal subjects. There was no evidence of precipitin-mediated hypersensitivity.

An Australian study by Finch et al (1973) carried out a multicentre investigation with sodium cromoglycate B.P. (Intal) as an etiological and therapeutic agent during the harvest season in 1972. Amongst those involved directly or indirectly in the wheat industry there is an unknown proportion of people who suffer from asthma or an exacerbation of asthma which is specifically related to the season of harvesting and the non-seasonal transportation and storage systems. There is often an associated rhinitis. The possible allergic etiology of the disease with mast cell involvement was investigated using sodium cromoglycate (Intal) as a diagnostic and therapeutic tool in an open assessment system. All patients had suffered from the ailment during the two previous harvests and did not complain of wheezing during the rest of the year. None of them were receiving any form of asthma therapy. Subject admission and

completion forms were utilized by the investigators. Intal was given with instructions to inhale four capsules per day for the duration of the harvesting, which was approximately one month. The study was beset by many difficulties not normally encountered in suburban areas. Distances, population dispersal, variable or poor harvests, the critical economic necessity of bringing in the crop and long working days added to the general problems found in any trial population. It is most unlikely that patients would or could be subjected to a double-blind trial as harvesting is one of the economic annual moments in their working years. The results lacking in the scientific or statistical merits of a double-blind trial are reasonably conclusive. Intal was effective in the prevention of the disease in most subjects and, as its only site of action is on the mast cell, then wheat farmer's asthma is mast cell mediated and probably of allergic origin.

Schrag (1971) reported that as part of a study to determine the ventilation requirements for various processes common in the grain industry, concentrations of airborne dust were measured in a number of feed mills, grain elevators, and a seed cleaning plant. The degree and effectiveness of exhaust ventilation employed varied greatly. The working conditions and sampling methods employed are discussed and indicated the variation in dust concentrations that may be found in Alberta's grain industry.

Gandevia et al (1966) measured ventilatory capacity before and after exposure to high concentrations of wheat dust in 24 men, 18 of whom were similarly studied while working with calcium phosphate rock. Changes in ventilatory capacity were examined in relation to respiratory symptoms commonly elicited in occupational surveys, and to the presence or absence of a productive cough on request and under observation. A significant decrease in the $FEV_1$ was observed within half an hour of beginning work in the wheat dust, and this decrease was maintained throughout the work shift. A smaller significant decrease was found on exposure to phosphate rock over several

hours, no significant change occurring within the first half hour. Greater or more consistent decreases were recorded in those men who gave a history of persistent cough and sputum, and more particularly in those who had a productive cough on request, than in those without these features. A history of symptoms on exposure failed to define a group showing any more severe ventilatory reaction on exposure to wheat dust than the average. Some of the factors influencing the history of symptoms in occupational populations are reviewed, and the advantage of an objective sign, as provided by a deliberated cough, is indicated in defining an 'abnormal' group within such a population.

Skoulas et al (1964) studied Saskatchewan grain elevator agents exposed to grain dust who developed respiratory symptoms such as cough, wheezing, breathlessness, etc., more frequently than the average population. Some employees even had to retire because of the severity of the symptoms associated with exposure to grain dust. An investigation was designed to determine the extent and nature of the conditions. The first part of this study included a survey of 502 grain elevator agents selected at random from the Province of Saskatchewan. One hundred and seventy-five of these agents were found to have a cough; other respiratory symptoms were reported less frequently. In the present clinical study 51 agents were selected initially from the 175 above-mentioned agents with symptoms (the ones who appeared to have the most severe symptoms according to the information in the questionnaire) and were classified as Group A. Grain elevator agents selected from the original group without symptoms were designated as Group B, and a third, small group made up of retired agents was designated as Group C. The main purpose of the present clinical study was to find the degree of functional disturbance and permanent damage, if any, in the group of grain elevator agents with symptoms as compared to the group without symptoms.

In an early Canadian study Williams et al (1964) investigated the high incidence of respiratory symptoms among country grain elevator agents. The study was undertaken in two stages: the first was a survey, by personal interview, of a

representative sample of country grain elevator agents in Saskatchewan with a view to estimating incidence, type, and severity of respiratory and other diseases in the group, considered to be related to their occupation; the second was a detailed clinical study of the men most severely affected, together with a group who denied symptoms and a few retired agents.

## Confinement Buildings

Thelin et al (1984) determined airborne dust and endotoxin levels on poultry farms, for various working processes known to involve a heavy exposure. Forty-seven workers at different sites were studied by questionnaires for work-related symptoms. Lung function measurements were made before and after work. Dust levels exceeded the standard for organic dust, and endotoxin levels exceeded those known to cause respiratory and other symptoms. The average decrease in $FEV_1$ over the working day(s) ranged from 0.07-0.19 litres. Upper airway irritation was present in one third of the workers, and about 10% complained of chest tightness. The effect may have been due to the high amounts of dust causing a general respiratory irritation as well as to the endotoxin.

Bar-Sela et al (1984) reported that 16 poultry workers with poultry house-related rhinitis and/or asthma underwent clinical and laboratory evaluation that included history and physical examination, skin tests with common inhalant and PAg, total- and specific-IgE levels, and pulmonary-function studies. Sixteen age- and sex-matched atopic subjects who were not occupationally exposed to poultry and 12 asymptomatic veterinarians with occupational exposure to poultry served as controls. Rhinitis and asthma developed only in symptomatic poultry workers after exposure to poultry; only in these individuals could immediate wheal-and-flare reactions to poultry antigens be detected ($p<0.001$). The elapsed time between the initial poultry exposure and the onset of poultry house-related symptoms averaged 10 yr.

In the symptomatic poultry workers, immediate skin test reactivity and RAST reactions were most frequently associated with NFM. The association between respiratory symptoms temporally related to poultry house exposure and the demonstrable IgE antibody-mediated reaction suggests a relationship between the two.

Jones et al (1984) made environmental measurements in three poultry confinement buildings in order to characterize gas and particulate contaminants. Levels of total and respirable dust averaged 4.4 and 0.24 mg/m, respectively. Particle size distribution as measured by cascade impactors was similar in the three confinement houses with a mass median aerodynamic diameter of about 15um and a geometric standard deviation of about 2.2. Ammonia levels measured in the active areas of the buildings averaged about 25 ppm. Ammonia concentration was quite high however, in an unused and unventilated portion of one of the buildings (x= 170ppm). $CO_2$ levels ranged from 0.05-0.1%. Levels of CO, $H_2S$, $NO_2$, $NO_x$, $CH_4$, mercaptan, formaldehyde, and hydrocarbons were all below the limit of detection for indicator tubes. Concentrations of airborne bacteria and fungi were on average about $1.5 \times 10^5$ and $1.0 \times 10^1$ colony-forming units/$m^3$ respectively. Endotoxin analysis was also performed on the total and respirable dust samples. Endotoxin levels (expressed in air concentration) ranged from 0.77 to 61ng/$m^3$ for total dust and from 0.71 to 15ng/$m^3$ for respirable dust. Endotoxin was also measured on the collection media from the individual impactor stages. Endotoxin was detected in all size ranges with the highest concentration of endotoxin per unit of dust found in the smallest (< 3.5um) size fraction. The endotoxin levels tend to be lower than those previously reported in poultry operations.

Lutsky et al (1984) examined the possible role of the northern fowl mite (NFM) in occupation-related disease of poultry workers. The study population included 16 poultry workers with workplace associated asthma and rhinitis, 27 atopic individuals with similar symptoms but no occupational exposure to poultry, and 12 asymptomatic nonatopic poultry-exposed controls. Ten of the 16 atopic poultry workers had immediate wheal-and-flare reactions to

NFM, as compared with two of 27 non-poultry-exposed controls ($p<0.001$). In cutaneous testing with five poultry-related antigens, the NFM was the most reactive. On skin tests, four atopic poultry workers were positive for NFM and negative for Dermatophagoides farinae; four workers were negative for NFM and positive for D.farinae. Radioallergosorbent test (RAST) showed specific IgE levels for NFM, with positive RAST scores in 60% of poultry workers having positive skin tests. A provocative bronchial test with NFM extract in a poultry worker having positive NFM skin test and RAST score resulted in an immediate 25% reduction in the $FEV_1$ and a 62% fall in forced expiratory flow volume at 25% of vital capacity. Collectively, the established presence of NFM in the poultry workplace, associated clinical histories, positive cutaneous tests, positive specific-IgE assays, and positive bronchial challenge combine to establish a role for NFM in occupational allergic respiratory disease of poultry farmers.

Lutsky and Bar-Sela (1982) commented on northern fowl mite (Ornithonyssus sylviarum) in occupational asthma of poultry workers and investigated the possible role of this mite in allergic respiratory illness in poultry workers. They studied 16 poultry farmers with a clinical history of allergic rhinitis, 13 of whom also had bronchial asthma. When at work in the poultry house all of them reported respiratory illness; however, outside this environment most of them noted a marked reduction in symptoms. Controls included 27 atopics with similar respiratory problems but not exposed occupationally to poultry and 29 non-atopics (12 with and 17 without occupational exposure to poultry). Scanning electron microscopy of selected samples confirmed the presence of mites and mite parts in poultry house dust. The presence of NFM in the poultry houses together with the clinical histories, positive skin tests and specific IgE assays, and positive bronchial provocation, establish O.sylviarum as a cause of allergic respiratory disease in poultry workers. The authors concluded that sustained exposure to the northern fowl mite may lead to significant workplace hypersensitivity and that this exposure may well be an occupational health hazard of

poultry farming.

Boyer et al (1974) surveyed 205 subjects involved in raising or processing turkeys for clinical and laboratory evidence of hypersensitivity lung disease. One hundred and forty-two (69%) described respiratory symptoms occurring within one hour after working with the birds. Thirteen workers (6%) also reported dyspnea, cough, myalgia, and fever occurring four to eight hours after exposure to turkeys. Sera from 11 percent of the study population contained precipitating antibodies against turkey serum, whereas 18 percent of subjects had positive skin tests to turkey antigens. When compared with the group of 63 subjects without complaints, the symptomatic group had a significantly higher prevalence of precipitating antibodies to turkey serum, positive skin tests to both turkey and environmental antigens, elevated IgE levels, and atopic histories. Many of the immediate onset respiratory symptoms were considered to represent type I immunologic reactions, whereas delayed symptoms were thought to represent type III reactions. This study showed that hypersensitivity pulmonary disease may occur in persons working with turkeys and that the delayed reactions closely resembled the same syndrome reported in pigeon and parakeet breeders.

O'Blenis, Nethercott et al (1984) reported a study for the Ontario Pork Producers Marketing Board of human health implications of working on hog farms. The study was divided into three parts involving an air monitoring study of six Ontario hog confinement farms, a detailed medical evaluation of 50 farm workers and a questionnaire survey of farm workers. Part A describes airborne contaminant monitoring in hog barns. A preliminary survey of six Ontario hog confinement farms was performed during March and April, 1983 to evaluate worker exposure to airborne dust, noise, ammonia, carbon dioxide, hydrogen sulfide, methane and carbon monoxide. Twenty-seven percent of personal total dust samples were greater than 10 $mg/m^3$ while fifty-three percent of the samples were greater than 4 $mg/m^3$. An exposure guideline of 4 $mg/m^3$ was considered to be reasonable since the major portion of the barn dust is feed grain. Three main factors contributing to worker dust exposures

were considered to be the hog feeding method, the feed grinding procedure and the individual work habits of the farm workers. Instantaneous sound level measurements were high during certain operations (e.g. feeding, working around tractors). Due to the intermittent nature of the noise exposures this resulted in only 2 of 21 personal dosimetry measurements exceeding 90dB(A). Measurements were made for ammonia, carbon dioxide, carbon monoxide, hydrogen sulfide and methane gases. Only one area at one farm had an ammonia gas level exceeding the present acceptable TWA exposure concentration.

Part B is a pilot investigation of the health status of 50 pork producers. There were a large number of potential health hazards to be evaluated including chronic effects of toxic gases, acute effects of toxic gases, respiratory and allergic problems related to dusts, noise-induced hearing loss, accidental injuries, muscle aches and strains (such as backache), rashes, stress-related disorders and possibly other health problems. The most serious of these problems is asphyxiation and death related to manure gases which are released by the agitation of manure. The gas is heavier than air and collects in a tank or pit either in the confinement unit or outside. Agitation occurs during mechanical movement of the waste, releasing noxious gases such as hydrogen sulfide. Although this is a specific hazard that all pork producers should be aware of, it is not one that occurs so frequently that it could be assessed as part of this descriptive study. Since the primary concern of the study was the health risks that may be generated by gases and dusts in confinement units, these were the focus of the investigation. Noise exposures were, however, evaluated in the field study part of the project and basic questions concerning the other health risks were asked in the questionnaire. The purpose of this part of the investigation was to document the health status of 50 adult pork producers. It was to yield detailed information regarding medical characteristics to supplement data obtained by way of a self-administered questionnaire which was sent to a large group of farmers.

In Part D (Note : Part C does not exist) the questionnaire survey is described. Its objectives were to investigate the

characteristics of hog farmers in Ontario, possible illnesses or conditions associated with hog production and to identify possible risk factors associated with such illnesses or conditions.

Recommendations are as follows :

1) Further study of hearing loss and noise exposure in Ontario pork producers should be carried out to document by audiometry and sound pressure level measurements the extent of this problem and what might be done to intervene and reduce this hazard

2) A further detailed examination of the pulmonary function of the small cohort of pork and dairy farmers who were studied in 1984 should be carried out in 1989 to establish whether significant chronic effects on respiratory function have occurred.

3) The nature and cause of the cutaneous problems in pork producers remains not entirely explained. An in-depth study of the approximately sixty farmers who reported skin disease should be carried out to elucidate the basis for their problems and what if anything might be done to prevent them. This would involve a further questionnaire survey followed by appropriate clinical examination and investigations such as patch tests and intracutaneous tests with components of the pork production process.

4) It is unclear whether the prevalence of knee complaints is excessive, but it is likely that it is. This should be examined further by a detailed study of the group of farmers who have knee problems to determine the type of knee problem, their effect in terms of producing disability and the causal factors which may have led to the problem within the working environment.

Donham et al (1984) tested a sample population of owner/operators of swine confinement production facilities by spirometry immediately before and after a 4-hr work period. These confinement workers had statistically significant decrements in flow rates ranging from 3.3% (mean FVC) to 11.9% (mean $FEF_{25-75}$). The air within the work environment was sampled for particulates and gases during the exposure period. There was suggestive evidence for a dose-response association between environmental exposures to carbon dioxide ($CO_2$) and hydrogen

sulfide ($H_2S$). There was also some evidence for an additive relationship between smoking and work environment exposure on decline in lung function. The results of this study indicate that those working in swine confinement buildings experience irritation to the respiratory tract which is manifested by decreased flow rates. These findings suggest this exposure represents an emerging occupational health hazard. Further studies are warranted to assess the potential for chronic or irreversible damage to the respiratory tract.

Donham et al (1984) initiated a study of possible chronic respiratory problems of people working in swine confinement buildings - a cross-sectional epidemiological study. A cohort of swine confinement workers was matched for age, sex, and smoking history with nonconfinement swine producers. Pulmonary function studies and a survey questionnaire for chronic respiratory disease symptoms (the American Thoracic Society), Epidemiologic Standardization Project Questionnaire) were performed on both groups. Compared to controls, the confinement workers experienced significantly higher prevalence of chronic bronchitis and wheezing, (odds ratio 7 and 4, respectively). There were, however, no significant differences in baseline pulmonary functions.

Based on the high prevalence of chronic respiratory disease symptoms, this study emphasizes an emerging occupational concern in agriculture to the estimated 500,000 persons working in swine confinement operations and the estimated 500,000 additional persons who work in poultry, veal, beef, or dairy confinemnt operations. It is important to study a representative population of these workers prospectively to determine if a progressive loss in lung function is evident.

The pathologic changes in laboratory animals housed in a swine confinement building were studied by Donham and Leininger (1983) to predict potential chronic health effects on persons working in these buildings. Rabbits and guinea pigs were maintained for 12 months either in a confined nursery-growers unit (test animals) or in conventional laboratory animal housing

(controls). Necropsies and histopathologic examinations were performed on animals that died prematurely or were killed at termination of the study. Blood serum from the animals was examined for antibodies to extracts from swine confinement house dust. The confinement atmosphere was monitored for environmental pollutants. Concentrations of gases and dust in the air of the confinement building were comparable to those found in a typical swine confinemnt building. Pulmonic lesions seen in the test rabbits and guinea pigs include diffuse interstitial histiocytic pneumonia. Tracheal and nasal turbinate lesions included epithelial hyperplasia and metaplasia, with submucosal infiltration of plasma cells and heterophils. Blood from the test animals contained serum precipitins to dust extract from confinement houses. The presence of precipitins combined with the microscopic appearance of the lungs indicated that an immunologic process, such as hypersensitivity pneumonitis, may be used to explain the basis of the observed lung lesions. The tracheal and turbinate lesions are best explained as a reaction to a chronic low-grade irritation.

Matson et al (1983) in order to determine the frequency and possible immunologic etiology of respiratory and other symptoms after hog barn exposure, studied 41 hog farmers and their family members. Participants completed questionnaires and provided serum samples for measurement of IgE and IgG antibodies to hog-derived antigens, hog feed, and hog barn dust. Symptoms after hog barn exposure were reported by 85% of the participants. Elevated IgE antibody levels to hog pelt, hog urine, and hog serum were found in only one individual; however, skin tests with these materials were negative. By radioimmunoassay, elevated IgG antibody levels to hog barn dust and/or hog feed were found in seven individuals; two of these sera contained precipitating antibodies to hog barn dust and hog feed. In no case could the presence of IgE or IgG antibodies be correlated with symptoms. Thus it appears that neither IgE nor IgG humoral immune mechanisms mediate respiratory or other symptoms in hog barn workers.

Harries and Cromwell (1982) report a case of asthma due to

occupational exposure to pigs. The cause of the symptoms was exposure to the urine of the animals. This was proved by provoking acute asthma with an inhalation challenge of an extract of pigs' urine at a concentration of 1 g/l. On a second occasion this asthmatic response was blocked by prior treatment with 40mg sodium cromoglycate (Intal). The patient's serum contained specific IgE antibody to the urine extract which was not found in unexposed controls.

Donham and Gustafson (1982) described the potential respiratory hazards associated with working in swine confinement buildings. Swine producers are the main users of the confinement system in the midwest. The use of swine confinement is growing in the southeast and near west. On an empirical basis, swine confinement seems to account for greater occupational concerns than confinement systems for other livestock species or poultry. Poultry confinement does not seem to elicit adverse symptoms in workers nearly as severe or as frequently as swine confinement. Beef cattle and dairy confinement systems are still relatively uncommon in comparison to swine confinement.

Donham et al (1982) present data to provide guidelines for the use of COHb measurement in swine as a means to monitor the environment in swine confinement buildings for potentially dangerous amounts of CO for swine and persons and to aid in the diagnosis of CO-induced perinatal disease in swine.

Katila et al (1981) tested 20 people employed in swine barns and 18 controls for sensitisation against dusts present in the barns. Immunoprecipitation and enzyme-linked immunoassay (ELISA) were used to test for IgG antibodies; IgE antibodies against swine epithelium were tested using solid phase radioimmunoassay. Precipitins against swine antigens were found in two swine workers, while ELISA found six to be sensitised. Sensitisation against swine antigens correlated with exposure but not with the presence of symptoms. No IgE antibodies were found. Precipitins against feed antigens were detected in 12 workers; in nine of the 12 with symptoms, and in three of the eight aymptomatic workers.

No single antigen was of special importance as an inducer of sensitisation. Sensitisation against feed dusts in barns, as indicated by the presence of circulating antibodies, suggests an immunological background for persistent symptoms. A large antigen panel should be used in testing for sensitisation because of the many immunogenic dusts present in the air in swine barns.

Mushroom Worker's Lung

Johnson and Kleyn (1981) described a patient with allergic alveolitis demonstrated by lung biopsy in a mushroom worker in Washington State presenting with severe airways obstruction. This is the first case of mushroom worker's lung reported in the United States outside the mushroom industry in Pennsylvania. The processes of commercial mushroom growing are discussed and the literature on mushroom worker's lung is reviewed.

Stewart (1974) reported the clinical picture, immunological findings, and working environment of six mushroom farm workers who developed the characteristic features of mushroom worker's lung while handling pasteurized compost.

A specific antigen has not been identified. The sporadic occurrence of the condition suggests that the antigen is present only intermittently in the working environment in sufficient concentrations to cause alveolitis. Until such time as the constitutional, immunological, and environmental factors predisposing to the development of alveolitis are better understood, preventive measures must be empirical.

Craig and Donevan (1970) reported respiratory illnesses believed to represent pulmonary hypersensitivity reactions, which occurred in two men employed in a large commercial mushroom-growing facility in eastern Canada.

Sakula (1967) described four cases of mushroom workers in Sussex (where 50% of English mushrooms are cultivated) who developed respiratory disorders thought to be related directly to their occupation.

Jackson and Welch (1970) described two cases of an acute chest illness occurring in mushroom workers. In one patient, who was severely ill, a lung biopsy was obtained which showed a pattern of alveolitis and interstitial fibrosis. The serum of both patients gave a precipitin reaction to an extraction of mushroom compost after spawning, but no reaction occurred to a variety of hay antigens used in the diagnosis of farmer's lung. A provocation test undertaken in one patient demonstrated a reaction to the inhalation of a dilute extract of mushroom compost after spawning. The most severely ill patient made a full clinical and functional recovery without steroid therapy.

Bunghurst et al (1959) collected clinical observations of 16 patients to exemplify a possible new disease entity. Each was a Puerto Rican migratory worker engaged in the handling of compost used as soil for growing mushrooms in Pennsylvania. The disease has not, as yet, been observed or identified in other persons. Immunity was conferred by a single episode or successive episodes. The disease recurred with re-exposure. Treatment was nonspecific and supportive. Removal of contact from the compost was necessary for cure. The consistent findings were respiratory signs and symptoms, characteristic roentgenographic appearance of lung fields, eosinophil count elevation, nationality of patient, and contact with the compost. The natural pattern of the disease resembles that of 'farmer's lung' and 'silo-filler's disease'. The etiology remains undetermined.

<u>Tobacco</u> <u>Planter's</u> <u>Disease</u>

Huuskonen et al (1984) studied a total of 57 subjects who had been exposed to mould dust in the tobacco industry. Their working environment showed exposure to spores of different moulds, and 29 subjects (51%) showed antibodies against one or more of the microbes. Fifteen (26%) had work related respiratory symptoms. Eight (14%) showed slight radiographic pulmonary fibrosis. Spirometry showed a tendency toward restriction and

obstruction, expecially in small airways. Diffusion capacity was decreased in 18% of the workers. Three clinical cases of typical allergic alveolitis were also found. All this suggests that exposure of spores of different moulds (especially Aspergillus fumigatus) in the manufacture of tobacco products may induce symptoms and signs relating to extrinsic allergic alveolitis.

Penneau et al (1982) reviewed tobacco planter's diseases. Tobacco is pathogenic for the consumer, and indeed his family, but he poses the question if it is also harmful to the cultivator and whether there is a professional pathology of tobacco planters. His evidence suggests it is.

Ghosh et al (1979) investigated occupational sickness among tobacco farmers due to the handling of green tobacco leaves, termed 'green symptom'. This symptom was investigated among 197 Indian tobacco workers and it was found that 88.83% of the workers were suffering from green symptom when exposed to green tobacco leaves during their occupational operation. Nicotine concentration of the urine was estimated only among male subjects who were smokers. During the exposure period (when subjects were suffering from green symptom), more than a three-fold increase in nicotine concentration in the urine was observed. Both cured and uncured leaves may cause such sickness.

Gehlbach et al (1979) observed that green tobacco sickness is an occupational illness of tobacco illness of tobacco harvesters that is thought to be caused by dermal absorption of nicotine from contact with green tobacco leaf. Wearing of rubberised nylon rainsuits effectively prevented nicotine absorption in volunteers who picked wet tobacco. Nicotine absorption was demonstrated in workers who wore clothing that was not waterproof.

Ghosh et (1980) al undertook an epidemiological study with X-ray, lung function, urine and blood tests to ascertain the incidence of 'green symptoms' among 290 tobacco workers handling cured or uncured tobacco leaves. The frequency of symptoms was very high (86.20 percent). The urinary excretion rate of

nicotine and its major metabolte, cotinine, was significantly increased in most of the cases.

Sprinchan (1978) commented on the fact that improved technology and labor mechanization bring with them much better conditions of work at new tobacco-raising complex economies. Working conditions at new mechanized installations for tobacco drying, on the other hand, are characterized by an unfavourable microclimate, pollution of the air with nicotinic fumes, methyl alcohol, ethereal oils, dust, etc. The tobacco dust contains admixtures of pesticides (cineb). The mechanization of labour processes in tobacco growing aids in reducing the expenditure of energy, but increases the role of the nervous-emotional load in performing work. Improved lay-out of premises and a better sanitary-engineering facilties, proper arrangement of the technological equipment and introduction of an adequate work and rest schedule, etc are needed.

Muminov et al (1977) reported that literature evidence pointing to the high percentage of the upper respiratory tract infection among workers of tobacco plants substantiated the necessity of studying the upper respiratory tract involvement in collective farmers engaged in preplant tobacco processing. Since hygiene conditions in different stages of tobacco processing differed, tobacco growers studied (528 in all) were divided into 4 groups, depending on the complex of chemical substances and dust acting upon them. The incidence of infections of the upper respiratory tract constituted from 87.5 to 90.5%, allergic rhinitis was diagnosed in 55.5% of cases. Complex examination of tobacco-growers by a dermatologist, neurologist, pathologist, and hematologist indicated occupational dermatitis in 26.5% of cases, functional changes of the nervous system in 56.3% of cases, and also the presence of thrombocytopenia and leukopenia. Thus, clincal characteristics of the upper respiratory tract infections, chiefly due to allergic and neurotropic action, and also the presence of correlation between diseases of the upper respiratory tract, the skin and nervous system, as well as hematological indices confirmed the toxicity of nicotine.

Gehlbach et al (1975) studied thirty-two workers on four North Carolina tobacco farms during harvesting. None of these workers smoked or chewed tobacco. Urinary cotinine (the major metabolite of nicotine) levels were monitored over a 24-hr period to evaluate nicotine absorption. There was a ten-fold rise in mean excretion of cotinine among workers who had greatest contact with the tobacco. Less cotinine was found in urine of workers who had less exposure. Levels of cotinine exceeded those found in novice smokers who smoke 3 cigarettes in succession. Absorption of nicotine from tobacco leaf is the likely cause of tobacco sickness.

Saakadze (1975) presents results of clincal examination and laboratory allergy tests in 1,700 tobacco industry and plantation workers. He discovered a high incidence of allergic respiratory disease (rhinopharyngeal disorders, rhinitis, bronchial asthma). A short period of sensitisation to tobacco is followed by a prolonged period of tolerance followed, in turn, by clear symptoms of allergy. Other occupational diseases induced by exposure to tobacco, but not of allergc origin, were also observed: atrophic or (more rarely) hypertrophic processes in the mucosae of the upper airways and chronic bronchitis (dust-induced or of complex etiology).

Gehlbach et al (1974) undertook a survey among 53 harvesters who had had green-tobacco sickness and 49 control harvesters to define and quantify the symptom complex. The illness was correlated with cropping (picking) the tobacco while it was wet; the absorption of nicotine from the leaf is the probable cause. Cigarette smoking affords protection against the disease.

Weizenecker and Deal (1970) investigated 'tobacco poisoning' or 'tobacco sickness'. Little was known about this illness by patients and nothing was found in the medical literature. Further inquiry revealed that, indeed, most of the lay public in this north central FLorida area knew of this entity. Several physicians in nearby counties also had treated patients in the past with the same chief complaint. To define this illness more

clearly, clinical and epidemiologic studies were initiated. Tobacco sickness occurs only in workers who allow staining of their skin by sap from Type 14 tobacco. Stringers and their assistants ordinarily do not become ill, presumably because they wear protective clothing. This illness is characterized initially by a feeling of generalized weakness, followed by severe nausea and protracted vomiting.

Sekerova (1969) reported that the diseases of the upper respiratory tract with temporary disability to work in Plovdiv tobacco manufacturing enterprises for the period Nov 1965 to Oct 1966 affected about 1/3 of the regular workers. This morbidity represents 36.8% of the cases of disease and 19.6% of the work-days lost because of disease. The workers in the shops handling tobacco and cigarette production suffer more frequently from catarrhs of the upper respiratory tract, the women, the young and recent employees being mostly affected. Morbidity of the upper respiratory tract with temporary disability to work shows a clear winter influence. The therapy and control of the diseased workers is carried out by therapists and other specialists and only in 7% of cases by an otorhinolaryngologist.

## CHAPTER TWELVE

## ANIMAL-BORNE DISEASES AND FARM WORK

### Introduction

Dr. Smith, Ministry of Health, Public Health Branch, presented to the MOA Task Force December 4, 1984 the number of cases of communicable diseases reported by local boards of health for the Province of Ontario and the rates of notifiable diseases per 100,000 population reported by local Boards of Health, for the eleven year period, 1973 - 1983, Ontario.

In a report for the Task Force on Health and Safety in Agriculture on the use of pharmaceutical products in farming and their potential for harmful health effects on farm personnel, Campbell (1984) comments that in modern livestock production the need for animal drugs for economic production of food is obvious. In addition to the retention of flock and herd health, with reduction of morbidity and fatalities, pharmaceuticals especially in the form of medicated feed are considered to afford up to 10% increases in growth and feed efficiency, and are extensively used. Indeed in the U.S.A. which has an agricultural system similar to that of Canada, it has been reported that 48% of all the antibiotics produced are used in agriculture. Concerns have been expressed regarding the potential public health risk incurred in their use. Little consideration has been given to the possibility of occupational hazards to those working with drugs on farms, and the regulatory areas of accountability for the control of the farm environment in this respect appears to be vague. The intent of this report was to discuss the roles of the various government agencies involved in the control of drugs in Canada and Ontario, the types of drugs used in farming, and areas of possible concern regarding potential risks to farm personnel involved in working in an environment of these products.

Parrish (1979) observed that at the present time, more than 130 animal diseases are known to be transmissible to humans. Fortunately, the majority of these present little exposure

because they do not usually occur in the United States; or the incidence rate is such that the risk can be effectively discounted.

<u>The Big Seven</u> are:

Anthrax
Brucellosis
Ornithosis (psittacosis or chlamydiosis)
Rabies (hydrophobia)
Swine erysipelas
Tetanus
Trichinosis

Fraser (1969) states that the main diseases which result from transference of infection from animals to man which occur in this country are tuberculosis, brucellosis, salmonellosis, anthrax, leptospirosis and a variety of viral and rickettsial infections. The incidence figures, geographical distribution, the infective agents and measures for the control of these diseases are given. The extent of the zoonoses in a community depends on the amount of infection in the animal hosts and the closeness of their contacts with man. Rural areas will thus score over urban districts and stock raising over arable farming.

## Bacterial Infections

Linnemann et al (1984) notes that the use of wastewater for agricultural purposes involves the potential risk of infection from microorganisms in the wastewater. The application of partially treated wastewater on farms has been reported in one study to be associated with human illness, but this has not been confirmed. In the present study, workers at a land application system involving low-pressure spray irrigation of corn fields with wastewater were followed through a growing season to determine if they had an increased risk of infection as compared with a control population of the same socioeconomic group who had no direct exposure to wastewater. Enteroviruses were recovered from the wastewater used for irrigation, but not from the air

during spraying. There was no increase in clinical illness among the workers and there was no evidence of an increased risk of infection. The workers who seemed at greatest risk, those who cleaned the spray nozzles, had higher antibody levels to one enterovirus, coxsackievirus B5, but acute symptomatic infections with viral excretion were not documented. This study indicates that there is very limited risk of infection among workers using partially treated wastewater for agriculture purposes.

Theddell et al (1980) presents a brief report of gram-negative bacterial endotoxin levels in airborne and settled dusts in animal confinement buildings. Gram-negative bacterial endotoxins, implicated in adverse worker health responses, were found in settled and airborne dust samples obtained from poultry and swine confinement units. Results of the Limulus amebocyte lysate gel test found endotoxin levels in dust samples ranged from 4.5 to 47.7 g of FDA Klebsiella endotoxin equivalents/gm. Differences in endotoxin levels between dust samples may have been due to variables in time, geographic locations, confined animals, confinement buildings and equipment, and methods of sample collection. Animal confinement workers are potentially exposed to large amounts of gram-negative bacterial endotoxins; however, the respiratory health effects of such exposures to animal confinement workers have yet to be determined.

Parushina et al (1977) looked at the problem of bacterial contamination of the work zone in the production of livestock products on an industrial basis. During the elaboration of the problem of developing efficient special work clothing for livestock breeding workers, the bacterial contamination of the atmosphere of production premises and washings from the integument and special work clothing of workers at one of the largest hog complexes in the country were investigated.

It was established that during the winter period 90% of the samples showed a continuous growth of microorganisms on Petri dishes and in the remaining samples the number of colonies in the air of the work zone reached 195,000 per cubic meter. Pathogenic staphylococcus was detected in 67% of the samples, and

nonpathogenic staphylococcus and streptococcus, in 33%.

Special work clothing stored in a warehouse for different periods was examined for bacterial contamination. It turned out that special work clothes laundered the day before and stored for 3-4 days and 1 month was contaminated with staphylococcus in like manner. It is significant that more microorganisms were detected on special work clothing and less on hands.

From the standpoint of labor protection for workers in livestock complexes the control of bacterial contamination in the production zone is mandatory.

The development of measures to prevent a bacterial effect on the worker's body should proceed in two directions: a) It is necessary to envisage in sanitary standards an indicator standardizing the content of microorganisms per cubic meter of the production zone of livestock barns. The introduction of this indicator into the standards of technological planning will make it possible at the stage of planning livestock complexes to envisage the most effective solutions for the creation of a sanitary and technical well-being in the production zone; b) It is necessary to accelerate the development of fabrics for special work clothing with stable and bacterial properties and improved physicotechnical characteristics.

Four cases of rickettsial endocarditis were presented at Clinicopathological Conference (1968). It had been amply confirmed that animals form the principal natural reservoir of the disease, though how man acquires infection from this reservoir was still rather obscure. In the U.S.A. cattle, sheep, and goats are infected, the organism localizing particularly in the placenta and milk of pregnant animals. Large numbers of organisms are then shed at parturition. The fact that they resist drying particularly well and have been isolated from the dust from clothing of farm workers, together with the fact that the vast majority of cases of acute Q fever present as acute pulmonary infections, makes it likely that infection in man is by inhalation of contaminated dust.

The patient described in Case 1 was a tractor-driver from Scotland, and the last published case of Q fever endocarditis also occurred in a Scottish tractor-driver. Here at least there

is a clear connection with rural communities and farming, but this is not always so.

Pernis et al (1964) investigated the role of bacterial endotoxins in occupational diseases caused by inhaling vegetable dusts. A large group of occupational diseases connected with the inhalation of various vegetable dusts, especially in the textile industry, have certain main symptoms in common such as fever, coughing, dyspnoea, and general malaise. In most cases the symptoms are more prominent on Mondays or on resuming work after one or more days of interruption. The symptomatology of these diseases and the Monday effect leads to the hypothesis that they are due to the inhalation of the endotoxins of gram-negative bacteria that contaminate the various vegetable materials, the Monday effect being connected with the phenomenon of tolerance to the endotoxins. Support for this view came from the demonstration of the constant presence of endotoxins in cotton dusts in textile mills and from the study of the effects of the inhalation of purified endotoxins in rabbits and man.

An outbreak of leptospirosis in cattle and man was reported by Hart et al (1984). On 20 May 1983 a 23-year-old dairy farmer became ill with headache and aching joints. His symptoms worsened during the next week, and he was admitted to hospital on 27 May because he was vomiting and had neck stiffness. He was thought to have viral meningitis; a lumbar puncture produced cerebrospinal fluid containing 300 lymphocytes and 30 polymorphs per l; protein and glucose were within normal limits. He was much better the next morning and was discharged on 29 May. He has remained well. His brother aged 20 took over the milking, and within the first few days he noted that five cows had an atypical mastitis, with a sudden drop in milk yield and clots in two or more quarters of the udder. On 1 July the farmer's brother developed an influenza-like illness. The epizootic nature of the infection in this herd and the possibility of further human cases led to a decision to treat the whole of the milking herd with single injections of dihydrostreptomycin at 25 mg/kg body weight and at the same time to give all treated

animals a primary course of two doses of a killed L hardjo adjuvant vaccine (Leptavoid-H, Wellcome). Since that time there has been no further illness attributable to leptospirosis on the farm. Cattle are the reservoir host for L hardjo, and persistent carrier animals maintain infection in the kidney. Infection probably entered this herd through the purchase of stock, possibly in May 1982, when the last group of adult stock was bought. A crop of abortions occurring in the autumn of 1982 was at the time shown to be mostly due to L hardjo infection, but no commercial vaccine was then on the market and treatment with dihydrostreptomycin alone has limited value in control. The cattle were turned out of winter housing in late April 1983, and during the exceptional rains in the spring of that year the wetness of the pasture is likely to have increased survival and facilitated transmission of infection. Cases of agalactia generally occur within a week or so of infection, but abortions usually do not follow for four to eight weeks.

Mackintosh et al (1982) reported a case-control study to investigate the correlation between titres to leptospiral serovars in workers and those in cattle in their herds. A total of 52 herds was investigated, 25 of which were 'high risk' where milkers had titres of 1:96 or greater, and 27 were case-controls where milkers had no detectable agglutinin titres at a minimum serum dilution of 1:24. The serological prevalence of titres to hardjo in cattle on 'high risk' farms (76.5%) was significantly higher ($P < 0.05$) than on the case-control farms (60.0%). The geometric mean titres of seropositive cattle on 'high risk' farms were also significantly higher ($P < 0.01$) than in the cattle from the case-control farms, especially in the younger cohorts. These findings suggest that there was active endemic hardjo infection in the two- to three-year-old cattle on the 'high risk' farms. Titres to pomona were demonstrated in only 5.2% of the cattle from both types of farm. Workers with titres to pomona tended to be from farms on which stock, especially calves, were bought-in and pigs were kept. Conventional measures for protecting milkers from contact with infected urine appeared to be ineffective and it is concluded that prevention of leptospirosis in dairy farm workers can only be achieved by elimination of infection in the

herd by vaccination of cattle.

The Leptospirosis Reference Laboratory and Communicable Disease Surveillance Centre (PHLS) presented a study of leptospirosis in man, British Isles, 1982. During 1982, 61 cases of leptospirosis were confirmed by the PHLS Leptospira Reference Unit, a number comparable with the average of 58 for the preceding three year period. Four of the patients died. Seven infections were thought to have been contracted abroad - two in West Germany, and one each in Brunci, Jamaica, Seychelles, south east Asia, and Spain. Of the remaining 54 cases, 16 were from the Republic of Ireland, three from Northern Ireland, and none from Scotland. The others were fairly evenly distributed throughout England and Wales. Nineteen of the patients were farm workers; all those specifically stated to have contact with cattle had hebdomadis (hardjo) infections, whereas among the 12 engaged in general farm work there were several icterohaemorrhagiae infections, doubtless due to exposure to rat urine. There were a further 10 infections in persons at known or probable risk of such exposure. These included an abattoir worker and a sewer worker.

The incidence of human leptospirosis in Israel which was 0.7 per 100,000 population was investigated by Shenberg et al (1982). The majority of the cases (62%) occurred in northeastern Israel (Upper Galilee). Prior to 1973 the main infecting serotypes were grip-potyphosa (41%) and Hebdomadis szwajizak (31%). Following the first outbreak of Hebdomadis hardjo infection in 1973, a change occurred in the epidemiologic pattern of human leptospirosis, with hardjo becoming the most common serotype (59%). Hardjo infection outbreaks were sporadic and localized to dairy farms. The peak of incidence was during the summer months, June-September. All the patients with hardjo were dairy workers. The illness was relatively mild and mostly unicteric. Cattle seemed to be the principal source of hardjo infection for man.

Lindebaum (1982) confirmed thirteen sporadic cases of human

leptospirosis due to Leptospira ballum during a period of 11 years. In four cases the diagnosis was proved retrospectively. All but three were residents of the Sharon plain region, living 10 to 15 km apart. All were engaged in some form of agriculture, especially in irrigated fields or groves, or in chicken farming. It was suspected that wet soil contaminated with the urine of rodents, carriers of L. ballum, was the main source of infection. Two types of immunological response were observed: 1) high microscopic agglutination (MA) titers with L. ballum serovar only (nine cases); and 2) considerble coagglutination titers with heterologous serovars as well (four cases).

Crawford and Miles (1980) observed four cases of illness attributed to Leptospira hebdomadis on a cattle farm in North Yorkshire. The clinical features were a febrile illness that resembled influenza; in one case there was a lymphocytic meningitis. This infection is probably more common than is recognised at present, and prevention of further cases may be possible if diagnosed promptly.

Olefir (1979) looked at the state of immunity of those in contact with mixed feed and microadditives. The absence of information about the influence of combined fodders and premixtures on the natural resistance and immunological reactivity as features defining the state of health of the workers was a cause for carrying out the mentioned investigations. Fifty-two workers of both sexes were examined (28 occupied in production, 24 in the preparation of premixtures). Seventeen people were in the control group. The age of those examined was from 20 to 39. In questioning the 56 workers and people of the control group they used a questionnaire proposed by the department of labor hygiene of the Central Scientific Research Laboratory of The Rizhskiy medical institute. Examination showed that in workers of the mixed feed shop of all comparable trades the bactericidal activity of the serum was decreased to $81.3 \pm 6.7$ with $21 \pm 1.2$ microbial colonies in the control ($P < 0.05$). The content of lysozyme in the saliva also decreased: a titer of $1:1367 \pm 105$ instead of $1:3450 \pm 390$ ($P < 0.05$). The level of lysozyme in the serum reliably dropped behind the analogous magnitude in the

control group ($36\pm4.4\%$) only in loaders, magnet operators, fillers and crushers ($22\pm2.7\%$). In workers occupied with the production of combined fodders and premixtures, a similar decrease of the absorptive and digestive ability of neutrophils, a decrease of the defensive properties of the skin, and a disturbance of the morphological composition of the blood were noted.

Torten et al (1970) describe an outbreak of leptospirosis. The outbreak which occurred in summer, 1968, involved mainly farmers engaged in open ditch irrigation. Serologic and isolation data showed that the main serotypes involved were grippotyphosa and mini Szwajizak. Epidemiologic investigation of possible vectors pointed to a large number of positive rodents, especially Mus musculus.

Henderson (1969) examined sera collected from dairy farmers, their families and farm workers; slaughtermen, artificial inseminators, veterinarians, and a group of doctors and civil servants with no direct connexion with farming for evidence of Q fever or leptospirosis. One thousand and fifty-two sera examined for Q fever yielded 26% of positive results with titres of complement-fixing antibody through 1 in 4 to 1 in 128 and over. On the other hand, 876 sera examined for agglutinating antibody to various leptospirae showed only 0.5% of positive titres of 1 in 80 and over. None of the individuals with positive sera for Q fever had ever been ill with anything resembling Q fever or could remember any ill health in the past; this suggests subclinical infection. One farmer with a high titre against L. copenhageni (icterohaemorrhagiae) gave a history of a recent febrile illness very suggestive of acute leptrospirosis. Infection due to leptospirae appeared to be very much less common than that due to C. burneti.

Martin et al (1967) reported on a long-term study of a farm with large and varied animal population. The primary purpose of the study was to examine the significance of leptospiral infections in a confined population, with known parameters. This

report describes the first year of the study of the domestic animal, wild animal, and human populations of the farm, where several serotypes of Leptospira were present.

Zourbas et al (1977) reported that on a three-stage sampling survey among farmers and their families living on farms in the department of Ille-et-Vilaine gave the following results: Among 490 persons examined 313 (64%) showed a positive skin test and 105 (21%) a positive serological reaction; 88 of the 105 patients ignored their health status, although 45 of these presented clinical symptoms (9%). This survey is continuing in order to study the non-respondents and analyse the epidemiological situation at a farm level.

Williams (1970) reports that in one area of South West Wales, thirty cases of brucellosis were presented over a 16-month period. Most of these patients were farmers or farmworkers, and two cases are described in detail. It is suggested that the risk of human infection with Brucella abortus has increased as a result of the accredited-herds scheme.

## Parasitic Infestations

Embil et al (1984) conducted a survey of. of Ascaris lumbricoides prevalence during 1976 and 1977 in a rural community of Nova Scotia. Of 431 individuals tested, 121 (28.1%) were infected. All those infected were under 20 years of age. There was no difference in the rate of infection between households with pigsties and those without. A significantly higher prevalence rate was found in homes where feces were disposed of in the yard and water was obtained from a dug well. In a concurrent random survey taken in the Halifax metropolitan area, none of the 276 individuals tested was infected.

Crellin et al (1982) reported on a descriptive epidemiologic study designed to test an impression that infections of Echinococcus granulosus in dogs, sheep, and human beings were concentrated in central Utah, and to determine when and how the

parasite was introduced into the state, which factors were involved in the distribution of the cestode, and which factors increased either a person's risk of infection or the number of people at risk. Data were secured by review of available records, interviews, questionnaires, and field observations. It was found that 37 of 39 infections in human beings, and seven of eight counties with endemic hydatid disease in dogs and sheep, are located in central Utah. Possible factors responsible for the increasing number of people at risk were use of local people as herders, the existence of comunity herds, and specific dog management practices. Determinants such as trailing sheep between seasonal pastures, association of sheepmen from several counties on winter range, and sheep marketing practices undoubtedly influence distribution of infections in dogs and sheep.

Palmer (1981) reported an outbreak of ornithosis in duck workers in the winter of 1979 and spring of 1980 discovered by the investigation of a cluster of cases in Norfolk. A serological survey showed that 61% of duck workers but only 23% of control poultry workers had chlamydia group antibody titres of > 1:8. Altogether 9% of duck workers in the survey had antibody titres >1:32 and a clinical illness suggestive of ornithosis. The proportions of seropositive tests and clinical attack rates were highest in workers eviscerating ducks and lowest in farm workers. It is suggested that a clinical history of contact with poultry should be considered relevant in the diagnosis of ornithosis and that clinicians caring for poultry workers should consider the possibility of ornithosis as an occupational disease.

Chmel et al (1976) describe a study of the occurence of T. mentagrophytes var. gran (ringworm) infection in small mammals living in nature and the possibility of the transmission of the aetiological agent from the natural focus of infection to man. The epizootological importance of small mammals is considered from the point of view of their ecological valency, an essential factor in the process of inter-species spread of infection. The

concentration of small mammals during winter months in the proximity of human dwellings is due to their search for food and shelter. The barns - the main work place of agricultural workers in winter - were found to contain the highest concentration of small mammals, of the most diverse species and biotopes. They are considered to be the main link in the process of transmission of T. mentagrophytes infection from natural foci to man.

French et al (1970) administered toxoplasmin skin tests to 237 residents of Riverside County, California, representing farm and non-farm groups, to determine if certain occupations are at higher risk of infection with Toxoplasma gondii. The agricultural workers had an infection rate of 39.6% which was significantly higher ($X^2$ = 10.1, D.F. = 1) than rates in cattle feedlot employees having intimate animal contact (9.4%) and county employees (14.4%). Serologic studies using the Jacobs dye-test method failed to reveal elevated antibody titers in the skin-test negative members of the cattle feedlot employees. Information on housing and sanitary conditions, method of preparing and eating meat, residence history and contact with domestic animals failed to show a significant correlation with toxoplasmin positivity. Possible explanation for the observed differences in toxoplasma infection in the various groups is discussed. The low rate of positivity in feedlot workers remains an enigma and calls for further investigation.

## Fungal Diseases

Vincken and Proels (1984) present what may be the first reported case of acute hypersensitivity pneumonitis due to Aspergillus fumigatus in vegetable compost. A previously healthy 20-year-old man presented with a three day history of dyspnea, dry cough, and fever. As his first job, he had started working two months before in a vegetable compost plant, where he had been repeatedly exposed to dust while turning the fermentation heaps with a garden fork. He was breathing shallowly and had fine crackles at both lung bases.

A chest radiograph showed diffuse bilateral reticulonodular

shadowing. The patient improved rapidly after his admission to hospital. On discharge from hospital, ten days after admission, the chest radiograph was normal. Three weeks later, six hours after a social visit from his work mates in work clothes, the symptoms and signs he had had at his first admission recurred and he was readmitted to hospital. The chest radiograph again showed diffuse, bilateral, reticulonodular shadowing with acinar consolidation in the perihilar regions. Four months after the first admission the forced vital capacity was 3.35 l, $FEV_1$ 29.1, and Kco 4 ml $min^{-1}$ mm $Hg^{-1}$ (1.3 mmol $min^{-1}$ $kPa^{-1}$). The patient changed occupation and remains well two years later.

The diagnosis of acute hypersensitivity pneumonitis was suspected because of the typical clinical course, the radiological features, and the occupational history of repeated heavy exposure to compost dust. Support for the diagnosis was provided by the relapse of hypersensitivity pneumonitis occurring within six hours of exposure to his work mates' clothes. Hypersensitivity pneumonitis occurring in farm workers who handle mouldy materials is almost invariably due to thermophilic actinomycetes, M faeni, or both.

Gilmore et al (1984) reported fatal pulmonary aspergillosis following a farm accident. They read with interest the recent report by Lake and associates that short-course corticosteroid therapy may be the only risk factor for developing disseminated aspergillosis. They recently cared for a previously healthy immunocompetent man with no known lung disease who developed fatal pulmonary aspergillosis after a two week course of corticosteroids. Unique to this case was antecedent trauma involving farm equipment. A 70-year-old farmer caught his right sleeve in the drive shaft of a manure spreader, trapping him against the machine for 15 minutes. This incident occurred on December 12, 1982. He was hospitalized for three days, for treatment of a brachial plexus injury. A chest radiograph on December 12 showed normal findings. On December 31, he was re-hospitalized for treatment of a three-day bout of chest pain and cough. The patient expired 24 days later secondary to respiratory insufficiency. A post-mortem examination was not

performed. They postulated that the prolonged entrapment in the manure spreader exposed their patient to a large inoculum of Aspergillus conidia and was the initiating event in the development of disease. Subsequent corticosteroid therapy rendered him immunoincompetent and resulted in overwhelming invasive disease.

Clark et al (1983) analyzed airborne dust in swine and poultry confinements to determine concentrations of total and gram-negative bacteria, total fungi, Aspergillus fumigatus and endotoxin. Airborne concentrations of total and gram-negative bacteria in swine and confinement units have been found to be as high as, or higher, than those found in other environments, such as wastewater treatment plants and cotton card rooms, where microbiologically contaminated organic dusts were present. Airborne endotoxin concentrations in the swine units (average 0.12 $g/m^3$) and poultry units (average 0.31 $g/m^3$) were in the range where clinical effects have occurred in other populations. They concluded that health studies of poultry and swine confinement workers with concurrent estimation of the individual daily exposure dose are warranted.

Peterson et al (1982) reported on two women (42 and 50 years old) in otherwise good health who presented with symptoms and signs closely resembling those of subacute or chronic bacterial sinusitis. Computed tomography disclosed localized involvement of one maxillary sinus in each patient. After surgical debridement and drainage, both patients became symptom-free and were without recurrence 6 months later. Most of the 111 other reported cases of benign, indolent paranasal sinus aspergillosis (which was diagnosed in these patients only upon examination and culturing of the surgical specimens) have been reported in agricultural areas having a hot, humid climate. The apparent increase in occurrence of these opportunistic fungal infections may be related to the increasing use of immunosuppressive agents and antibiotics. The fulminant, invasive form of paranasal sinus aspergillosis typically occurs in patients severely debilitated by systemic diseases (notably leukemia) and/or immunosuppressive treatments.

The potential hazard from inhalation of aflatoxins in airborne dust to agricultural workers handling contaminated corn was investigated by Burg et al (1981). Aflatoxins are a group of chemically similar compounds, bis-difurancourmarins fused to either a pentenone (B-series) or lactone ring (G-series), which are metabolites of two common fungi: Aspergillus flavus and Aspergillus parasiticus. Several of these compounds have been shown to be highly toxic, mutagenic, carcinogenic, teratogenic, and immunosuppressive in animal studies.

Sneller et al (1979) surveyed a predominantly agricultural community in California for prevalent fungal spores during a 12-month period. Alternaria, macrosporium and stemphylium were recovered during asparagus and strawberry harvesting times year-round. Fusarium and botrytis were less frequently associated with the strawberry harvest and were recovered only during the first quarter of the year. Epicoccum was recovered in the north end of the Salinas valley in low numbers throughout the year and was strongly associated with the strawberry and artichoke harvest. Aureobasidium (Pullularia) recovery occurred in different locations according to season, correlating somewhat with the cabbage harvest as well as with the harvest of strawberries. Recovery of the pigmented yeasts showed strong correlation with the local growing season for lettuce. Cladosporium was prevalent year-round but did not appear to be significantly affected by changing agricultural conditions. These data have permitted the predictability of mold aeroallergens with medical applications.

Emanuel et al (1975) commented that mycotoxicosis is a term used to define a toxic reaction due to the ingestion of toxins produced by fungi. Oral ingestion, however, may not be the sole means of exposure. We have recently observed ten patients who had inhaled massive amounts of fungi, which resulted in an apparent toxic pulmonary reaction. Immunologic studies showed no sensitivity to various fungal antigen preparations and histologic study of the lung showed a multi-focal acute process, with

primary involvement of the terminal bronchioles containing large numbers of various spores. Cultures from lung biopsy material revealed at least five fungal organisms. A one to ten year followup indicates that avoidance of massive reexposure to fungal dust is the key to the prevention of recurrent pulmonary mycotoxicosis.

## Viral Infections

Mergler et al (1982) reported on warts among workers in poultry slaughterhouses in Quebec. The objective of the study was to identify the prevalence of warts in poultry slaughterhouses. A questionnaire was administered to 1,194 workers, of whom 569 completed it. The prevalence of warts (Papilloma virus) was found to be 28.5% in slaughterhouses. In the general population it is 7-10% reaching a peak in individuals around the age of 14 a. In the poultry slaughterhouses, the prevalence was highest (38.7%) in the age category 25 - 29 a, and among those who had been working 4 to 6 a (40.8%). The factors present in the work environment that showed a significant correlation ($a \leq 0.05$) with the presence of warts were the following: steel-mesh gloves that were too large for the wearer, work with a saw, handling of cold objects, and high humidity levels. It was concluded that mild abrasion of the skin (too-large gloves) and high humidity facilitate cutaneous infection by the virus, whereas the handling of cold objects and work with a saw provoke local vasoconstriction which could hinder the immune reaction.

Shelley and Shelley (1982) reported that inasmuch as orf, milker's nodules and bovine papular stomatitis pox are clinically identical in man and are induced by currently indistinguishable papapox viruses, they propose a new generic term 'farmyard pox' for these diseases. This affords the clinician a diagnosis based on a common set of clinical and electron microscopic findings rather than one based on an uncertain or even misleading history.

Murray B. Gardner (1982) in "Viruses as Environmental Carcinogens: an Agricultural Perspective" considered four major families of viruses associated with cancer in animals and man, and highlighted the exogenous cofactors and related preventive measures. He mentioned those agricultural practices that have resulted in significant economic loss from virus-induced cancer in farm and domestic animals and summarized some of the occupational hazards from environmental agents other than tumor viruses. There are four major families of viruses associated with cancer in animals; 1) retroviruses, 2) herpesviruses, 3) papovaviruses, and 4) hepatitis B virus. Retroviruses have not yet been incriminated in human cancer despite extensive research.

The animal retroviruses apparently present only the remotest public health risk. Herpesviruses are associated with naturally-occurring kidney cancer in the frog and lymphoma in rabbits, chickens, and New and Old World monkeys. In humans, the Epstein Barr virus is associated with Burkitt's lymphoma and nasopharyngeal carcinoma, and the herpes simplex virus with cervical carcinoma. Cytomegalovirus is associated with Kaposi's sarcoma. As with retroviruses, the herpesviruses are also ubiquitous, usually latent and nonpathogenic. They are spread by solely horizontal means and usually held in check by the host's immune response and genetic resistance at the cellular level. The major environmental factors associated with Burkitt's lymphoma in man are an early age of infection and coincident malaria. Nitrosamines, herbal drugs, and noxious fumes have been suggested, but not confirmed as cocarcinogens for EBV-related nasopharyngeal carcinoma. None of the animal herpesviruses are infectious for humans. Members of the papilloma virus genus are ubiquitous in many mammalian species including man in which they induce benign epithelial or connective tissue tumors that regress and are highly host and tissue-specific. Papillomaviruses in rabbits, cattle, and man can be associated with squamous cell carcinoma. None of the animal papillomaviruses are infectious for man. At least six different species of papillomavirus cause skin, anogenital and laryngeal warts in humans. Life-long persistent infection with hepatitis B virus is a major risk factor for development of chronic active hepatitis, cirrhosis, and primary hepatocellular carcinoma. This tumor is relatively

rare in the U.S.A. and Europe, but it is the most common cancer of males in parts of China, Taiwan, southeast Asia, and most of Africa. Chronic carriers, which make up 5 to 20% of these high risk populations, usually arise as a result of neonatal infection acquired from their mothers or siblings who are also chronic carriers. An immune response to the persistent HBV infection results in continuing damage to infected hepatocytes. Continuous liver-cell regeneration results which likely sets the stage for cocarcinogenic interaction with other environmental carcinogens. Aflatoxin B, a mycotoxin that commonly contaminates peanuts, grains, and human foodstuffs; aklaloids in medicinal plants; and nitrosamines are the most probable candidates. Prevention might be aimed at eliminating aflatoxin from the areas involved, but this would require major changes in the economics and agricultural practices. It should eventually be possible to completely eradicate HBV infection and associated PHC in this high risk population by use of a vaccine program. In conclusion, retroviruses are widely prevalent in animals, but are seldom pathogenic. Close crowding and poor hygiene enhance the opportunities for horizontal spread of the viruses early in life and allow for them to "get a jump" on the immune system and establish the chronic carrier state. From the agricultural standpoint, closed or semiclosed containment of animals (such as chickens or cows or cats) is a major culprit fostering spread of herpes, papova, and retroviruses. Selective breeding of farm animals for economically favorable attributes, such as rapid weight gain, may also increase their genetic susceptibility to these agents. Vaccine induced protection against the naturally-occurring virus-associated tumors is a proven value with lymphoma and breast cancer in mice, lymphoma in cats, Marek's disease in chickens and hepatitis in man. Reduced exposure to important cofactors, such as bracken fern, improved hygiene, and more "breathing room" may be equally effective in prevention of the associated tumors. The animal tumor viruses are highly species-specific and are not infectious for humans. Even in high exposure situations no convincing evidence exists for even a single human infection, past or present, with any of the animal tumor viruses. There is, thus, no reason to consider the animal

tumor viruses as public health risks. By contrast, occupational hazards for farm workers from environmental agents other than veterinarians, and lab technicians face possible injury from accidents, bites, or scratches, in addition to infections from animals or their ectoparasites. Infections caused by farm animals include tuberculosis, anthrax, brucellosis, leptospirosis, salmonella, streptococcus, staphlococcus, Q fever, and viral or fungal infections. Recent outbreaks of ornithosis in veterinarians from exposure to ducks, in poultry processing plants are a pertinent example. The current revolution in biotechnology and introduction to agribusiness of advanced techniques of genetic engineering raise exciting prospects, but also some cautionary notes. As more and more commercial livestock and cat breeding operations take place in crowded, closed, or semiclosed units we can anticipate further outbreaks of leukemia, papillomatosis, and other infectious diseases among animals and increased exposure of farm workers to the other occupational hazards mentioned above.

Donham et al (1977) conducted a seroepidemiologic study in an attempt to identify antibodies against the bovine leukemia virus (BLV) in people exposed to cattle with lymphosarcoma. Farm families, farm employees, and veterinarians in contact with cow herds having documented cases of lymphosarcoma were tested for precipitating antibodies to the BLV with the agar gel immunodiffusion test. The cattle also were tested serologically. Information was collected from the farm families regarding consumption of unpasteurized milk from their dairy herd. Twenty-one dairy herds with documented cases of lymphosarcoma were identified. A total of 846 cows from these herds were bled, of which 33% were serologically positive. No positive sera were found in the 45 dairy farmers, family members, and farm employees associated with the herds with lymphosarcoma. Consumption of raw milk was reported by 77% of the farm group. In addition, 83 veterinarians, 30 leukemia patients, and 200 control human sera were tested and found negative for antibodies to the BLV.

Caldwell et al (1976) investigated the possibility that FeLV

and BLV might be transmitted to people. With regard to the BLV study, the basic plan was similar to the first survey as far as specimen collection, interviews, and serologic testing were concerned. It differed by dividing the population into two groups, one group in contact with BLV-positive herds and the other in contact with BLV-negative herds. The preliminary data raises the possibility that FeLV may cross the species barrier to man and elicit an immune response. The significance of this finding is not clear at present. No increase in cancer incidence was found in the study population, and previous epidemiologic studies are contradictory. Further study of FeLV and its relationship to human disease is warranted. There is no evidence that BLV either crosses the species barrier to man or that bovine leukemia is associated with human cancer.

# CHAPTER THIRTEEN

## FERTILIZERS AND NOXIOUS GASES

### Fertilizers

Davis (1984) observed that in intensively populated countries efficient sewage treatment is essential to protect river quality. An inevitable by-product is sewage sludge which has to be disposed of safely and economically. Utilisation of sludge as a fertilizer of agricultural land is the most economic disposal route for inland sewage-treatment works and also benefits farmers by providing a cheap manure. Much of the cadmium in wastewater is concentrated into sludge which consequently contains higher concentrations of cadmium than soil does. It is impracticable to reduce cadmium concentrations in sludge below certain levels. When sludge is used on farmland rates of application must be controlled so that cadmium concentrations in soil never reach levels that could significantly contaminate food crops. Cadmium is a principal factor limiting the use of sludge on land. Nevertheless, it is a local problem since agricultural land in general receives more cadmium from aerial deposition and phosphatic fertilizers. The significance of accumulations of cadmium in soil depends mainly on its availability for crop uptake. Investigations are described which have attempted to identify and to determine the availabillity of forms of cadmium in soil. There is considerable research interest in cadmium in soil solution which is likely to be directly available for crop uptake. Another area of interest is the apparent disappearance of cadmium from sludge-treated soil. Soil analysis often cannot fully account for the cadmium added in sludge. Apart from the effect of soil conditions, especially pH value, crop uptake varies according to the particular crop examined. Highest concentrations of cadmium occur in tobacco, lettuce, spinach and other leafy vegetables. Using crop uptake data from field trials it is possible to relate potential human dietary intake of cadmium on which hazard depends, to soil concentrations of cadmium, which can be controlled by regulating applications of sludge. This provides

an objective basis for limits for cadmium concentrations in soils receiving sludge. Transfer of cadmium via farm animals to meat and dairy products for human consumption is thought to be minimal, even allowing for some direct ingestion of sludge-treated soil by the animals. Evidence from these and other investigations suggests that a loading rate limit of 5 kg Cd/ha (equivalent to a soil concentration of about 3.5 mg Cd/Kg) affords adequate protection to the foodchain where sludge is used on agricultural land. More research work is needed to provide a basis for predicting the long-term availability of cadmium introduced to the soil in sludge.

Guerin (1983) observed that a farm boy aspirated liquid barnyard manure during a seizure. Findings, treatment, and course are described for this previously unreported phenomenon.

King et al (1982) summarized the explosion hazards of ammonium nitrate and ammonium nitrate-based fertilizer compositions. Ammonium nitrate is manufactured, stored and transported in very large quantities in Canada and worldwide. The European Economic Community was the first in recent years to move towards establishing a basis for determining which of those varieties of ammonium nitrate fertilizers currently manufactured and transported were unduly sensitive to shock. The Council of the European Communities, proposed to determine at the Community level the characteristics and properties distinguishing ammonium nitrate based fertilizer from products based on ammonium nitrate manufactured for use as an explosive. To this end a directive was drafted and submitted to the European communities which contained among new regulations regarding coatings and fillings for ammonium nitrate fertilizers of high nitrogen content, a series of tests to determine porosity, pH, size analysis, chlorine content, combustible material content and a <u>detonability test</u>.

Donham et al (1982) analyzed a mail questionnaire to a sample of swine producers that indicated that more than 85,000 people in Iowa and an estimated 500,000 in the United States work

in livestock confinement systems that use liquid manure storage. Deaths and illnesses in people with acute exposure to toxic gases emanating from the liquid manure have been recently reported. This communication reports results of the investigation of six such incidents. Hydrogen sulfide appears to be the main toxic substance involved, and agitation of the liquid manure is important in creating an acutely severely toxic environment. Preventive measures must include worker education and limitation of human exposure through control of environmental and human factors.

Turek (1982) commented that on the basis of long-term observation it has become obvious that there is an increasing content of nitrates in the plants, which is reflected in the values of nitrates in the urine of humans. Other investigations draw attention to the importance of selection of sorts, careful application of fertilizers and introduction of other measures in an attempt to solve the problem.

Fraser et al (1982) investigated whether exposure to nitrate-containing dust during fertiliser manufacture was associated with an excess of deaths from cancer in general or specifically from cancers of the digestive tract, liver, lung, and bladder. It was based on data extracted from census schedules by the Office of Population Censuses and Surveys, occupational characteristics recorded by fertiliser workers at the 1961 and 1971 censuses of England and Wales being related to subsequent mortality ascertained through the National Health Service Central Register. The 1961 cohort, followed up until 1978, showed a "healthy worker effect" and no evidence of excess mortality from cancer at any site. The 1971 cohort also showed below average mortality during 1971-77 for all causes of death and for circulatory diseases, but there were more deaths from cancer than expected, due mainly to an excess of cancers of the lung and digestive tract. The excess of cancer was more pronounced, but not statistically significant, when compared with other employed men. Though the numbers for comparison were small, there was weak evidence of an association between cancer mortality and frequency of exposure to nitrate-containing dust in

this cohort. It is difficult to reconcile the excess cancer mortality in the 1971 cohort with the more favourable level in the earlier cohort, since industrial hygiene has improved and the cohorts showed a similar distribution by region and social class. To examine further these conflicting results the 1971 cohort will be followed for a longer period and re-examined when more deaths have accrued.

Osbern and Crapo (1981) observed that the use of liquid manure storage facilities poses several serious threats: toxic gas inhalation, asphyxiation, aspiration of liquid manure, and infection. Hydrogen sulfide poisoning in a manure storage pit resulted in three deaths. Two of the persons who died had massive aspiration of liquid manure; the third had severe pulmonary edema but had not aspirated manure. The clinical course of the patient who survived was complicated by hemodynamic instability, adult respiratory distress syndrome, and infection. These accidents can be prevented by the use of a self-contained breathing apparatus and a safety line, as well as the presence of a second person for rescue if necessary. Recommendations for treatment are mainly supportive, including cardiopulmonary resuscitation, mechanical ventilation, oxygen, and positive end-respiratory pressure. Nitrites may speed recovery but in excess can cause other complications.

Phillip et al (1979) determined the occupational exposure of single persons due to the gamma radiation of the natural radionuclides in rock phosphates and phosphate fertilizers and their contribution to the population dose in the FRG. The exposure rates in the working fields production, transport, loading and storage of rock phosphates and phosphate fertilizers and due to their application in agriculture have been measured by means of scintillation dose rate meters of LiF-thermoluminiscence dosemeters or have been estimated from specific activities. Mean additional exposure rates of 2-26 R/h, with local maximum values up to 190 R/h, were observed. From these values, together with statistical data for the number of occupied persons and annual working times in the various

working fields, the mean and maximum annual dose of individuals and the contribution to the mean poulation dose have been estimated. The results show 45 mrem/y (production plants or storehouses) can occur. The corresponding mean annual doses are 0.05 - 20 mrem/y. The contribution of the occupational radiation exposure due to rock phosphates and phosphate fertilizers to the mean population dose is 1274 man.rem/y related to whole body. To this, fertilizer production contributes 40 man.rem/y, transport and loading 45 man.rem/y, agricultural storehouses 31 man.rem/y, and agriculture 58 man.rem/y. Altogether, this investigation shows that an occupational radiation exposure of individuals may occur which corresponds to the mean terrestrial radiation exposure in the FRG. The contribution of the occupational collective doses due to phosphates to the population dose, however, is negligibly small.

Fabri et al (1978) examined one hundred and ninety subjects employed in the production of phosphate and compound fertilizers; for each subject a respiratory symptoms questionnaire (standardized by the European Carbon and Steel Community) was completed, and lung volumes and CO transfer in steady state were measured. High rates of chronic bronchitis (36.8%) and obstructive functional impairment (46.3%) were observed in the whole group. Separate analysis of the results regarding workers employed in each individual production cycle revealed a higher prevalence of impairment in those exposed to fluorinated gaseous products. There is obstruction, with reduction in CO transfer in steady state which can be attributed to changes in the ventilation-perfusion ratio. The origin of the functional changes and chronic bronchitis can be traced to the simultaneous exposure to dusts and irritating gases which exert a synergic action on the respiratory apparatus. The results demonstrate the need for a revision of the present maximum permissible limit for fluoridric acid and for the establishment of permissible limits for hexafluosilic acid and silicium tetrafluoride.

Nielsen et al (1978) presented a report of saltpeter-induced calcium deposits in ten patients who showed a close clinical and histopathological similarity to the lesions of pseudoxanthoma

elasticum. By electron microscopy and selected area diffraction analyses of the calcium deposits they found the changes indistinguishable from the changes, in involved skin of patients suffering from PXE. Ten elderly farmers from Denmark and Sweden all presented the same history: 30-50 years ago, while fertilizing, they spread Norwegian Hydrous Saltpeter with their hands. Their shirt sleeves were rolled up over the elbow and the weather was damp or foggy. After spreading thus for some hours they felt a burning skin sensation and soon corrosive ulcers formed. One of the farmers developed corrosion ulcers on his legs located by the upper parts of his rubber boots.

It is surprising that an industrially produced fertilizer such as Norwegian hydrous salpeter can induce eruptions clinically very similar and light microscopically indistinguishable from PXE.

Jindrichova et al (1977) commented on hygienic conditions in workplaces, especially the dust concentration, were evaluated at 6 fertilizer mixing plants (potassium chloride, superphosphate, ammonium sulphate). Due to insufficient mechanisation when unloading and further processing of the fertilizer without proper dust protection measures, the dust concentration at the workplaces amounted to as much as 911 mg of dust/$m^3$ air. 14 people with an average age of 28 years were examined. They were exposed in the workplaces on average for 4.9 yr and none of them underwent an entry examination when they began to work there. Besides diseases contraindicated for work in a dusty environment (chronic bronchitis), grey pigmentations on the mucosa of the nasal septum and hypertrophy of the septum mucosa were ascertained in 2 men, pharyngitis granularis in 1 and toxic eczema of the hands and face in another.

Jedrychowski et al (1977) investigated the influence of working conditions - with particular reference to dust and fluorite pollution - on the epidemiology of chronic bronchitis in 197 subjects working in a fertilizer producing plant in Krakow (Poland). The investigation included history, respiratory function tests (VC, TVC), height and weight measurement, rhinolaryn-

gologic examination, nasal mucosa cytology and physical examination. The environmental survey included measurements of the dust respirable fraction and fluorite concentration in the air. The prevalence of chronic bronchitis was found to increase with the length of working activity and to be much higher in smokers than in non-smokers. Furthermore, in subjects working at the sites with the worst environmental situations it proved to be twice as high as in the reaminder. Likewise higher proved to be the prevalence of laryngitis and sinusitis. The prevalence of chronic bronchitis was found to be much higher in workmen with more marked spirometric changes. In subjects affected with chronic bronchitis alterations of the nasal mucosa epithelium were also found.

Fletcher (1974) reviews ammonia accidents: prevention and care. most accidents involving ammonia occur when either the liquid or gaseous ammonia gets in contact with the skin or eyes of the victim or is inhaled in excessive quantity. Fortunately, the odor and irritating sensation caused by ammonia will drive any person to leave the area of contamination. If trapped, excessive inhalation will cause lung irritation, and paralysis of the diaphragm. Ammonia has a strong affinity to water, rendering the eyes especially vulnerable as they are always moist and lack the protection of normal skin. The material will cause a caustic burn of the eye tissue if not treated immediately by water flushing. If the injury is sufficient to affect the lens of the eye, some - or perhaps total - loss of sight is almost inevitable.

Helmers (1971) observed that as with many technological advancements of our society, ammonia fertilizer possesses the potential for serious injury to man, and even self-destruction. A mishap involving ammonia will usually cause the victim great pain and loss of time and may well rob him of his eyesight if the contact with the material is on his face. The hazards of ammonia have been well investigated because of its long use as a refrigerant; however, it is relatively new to the farmer and to his treating physician.

## Miscellaneous Gases

Matthews (1967) discussed some measurements of carbon monoxide pollution of glass-house atmosphere during mechanized cultivation. The measurements of atmospheric carbon monoxide and blood concentration of carboxyhaemoglobin to emphasize the potential hazards of this work for the operator. Symptoms of extreme exposure (i.e. dizziness or headache) were experienced and correspond with the effects predicted for the range of maximum atmospheric concentrations measured and the durations of work with the machines. Obviously the method of preparation for this work on some holdings, where lights and doors are not fully opened, is not satisfactory.

Minimum precautions necessary are:-

(a) All doors and lights must be fully opened.

(b) The work should preferably be done on a day with the least winds.

(c) At first sign of any of the symptoms of excessive carbon monoxide exposure - dizziness, nausea, weakness, headache - no further work should be attempted with a petrol-engined machine for the remainder of the day.

## Gasoline and Diesel Fumes

Ohnishi et al (1980) reported that using the Ames Salmonella (typhimurium TA98, TA100, TA1535 and TA15381 rat liver)-microsome system, mutagenic activity was detected in the exhaust from 2 kinds of 4-cycle gasoline engines of unregulated and regulated cars, and from diesel engines, and in the particulates from air collected in tunnels. The mutagenicity of particulates from a car equipped with a catalyst (regulated car), as compared with that from an unregulated car, was reduced very much (down to 500 from 4500 revertants/plate per m3 in tester strain TA98). The mutagenicity of the ether-soluble acid and neutral fractions from the condensed water of emissions from a regulated car was still high (down to 2880 from 10,900 revertants/plate per m3 in tester

strain TA100). The mutagenic activity of emission exhaust from old diesel car engines was very high; the particulates showed 9140 and 19,600 revertants/plate per m3 from strain TA98 incubated with an activating rat liver S9 fraction. A small diesel engine of the type used for the generation of electric power or in farm machinery also produced exhaust with highly mutagenic particulates. The mutagenic activity of a methanol extract of particulate air pollutants collected in a highway tunnel showed 39 revertants/plate per m3 toward strain TA 98 and 87 toward strain TA100. The ether-soluble neutral fraction yielded 86 revertants/plate/m3 from strain TA 98 and 100 from strain TA100. This fraction also contained carcinogenic compounds, including benzo(a)pyrene, benzo(e)pyrene, benz(a)anthracene, and benzo-(ghi)perylene and chrysene. Very high mutagenic activity was detected, especially in the particulate air pollutants collected at night, in another tunnel on a superhighway: 60-88 revertants/plate per m3 from strain TA100 for the sample collected by day, but 121-238 by night. Night traffic includes many more diesel-powered vehicles compared with gasoline-powered automobiles.

Schenker (1980) reviewed the existence of polycyclic aromatic hydrocarbons (PAH) in the particulate phase of diesel engine exhaust which has raised concern about a carcinogenic effect in workers exposed to exhaust from diesel engines. Some of the PAH are carcinogenic following inhalation by experimental animals and are associated with excess cancer mortality in some occupational exposures. Studies of occupational exposure to diesel exhaust show concentrations of PAH are above ambient levels but below the very high levels in occupations with demonstrated excess cancer mortality. A critical review of the epidemiologic evidence on the carcinogenicity of workplace exposure to diesel engine exhaust is suggestive of a carcinogenic effect but the existing data are sparse and contradictory. Further epidemiologic studies of this question are needed.

## CHAPTER FOURTEEN

## PHYSICAL HAZARDS AND FARM WORK

### Accidents

Farming is a dangerous occupation. Although the farmer tends to be healthier than his urban cousins, he is faced with an array of mechanical hazards that can cause injury and death. His machinery can do irreparable harm to a limb in very short order. His animals are unpredictable. His silos and barns have hidden dangers and his tractor may be a death trap.

The character and face of farming in Ontario have changed greatly in the past 20 years. There are fewer small, family farms, and the farm population has dwindled as larger, more heavily mechanized and efficient farms have emerged. In order to survive financially, the farmer has perforce become more sophisticated in his operations. There is a much greater reliance on paid employees than in the past.

Baker (1981) did a review of research in farm accidents. A true understanding of the depth, scope and severity of the farm accident/injury problem requires an appreciation of the current state-of-the-art literature in the field. Thirty-two articles were reviewed representing Canada and the United States. Each Country was reviewed separately, with the articles appearing in chronological order of their publication.

In Canada although the hazards and dangers of farming have been long recognized by government departments, safety association, farm/farmer organizations, and a handful of interested persons, little research into the determinants and consequences of farm accidents has actually taken place.

A hypothesis held by the Government of Ontario, Ministry of Agriculture and Food is that 'youthfulness' is a 'cause' of farm related accidents/injuries. If this is correct, the association between risk and (young) age should become apparent in the course

of the inquiry. No association was detected between the age of the respondent and accident/injury involvement, either in the interview or mail survey group.

Sex, Marital Status, County of Residence/Employment, Farm Safety Association Membership, and Level of Education Attainment revealed no association with involvement in an accident/injury event.

The Ministry of Agriculture and Food has intimated that an association does exist between accident/injury involvement and being a farm employee, as against an owner. The Farm Safety Association has, on the contrary, intimated an association between accident/injury involvement and being a farm owner. Data from the mail survey group provides weak support for the former view, the personal interview group provides weak support for the latter. Thus the present inquiry found no systematic association between farming status (employer:employee) and accident/injury involvement. There appears to be a strong negative relationship between length of farming experience and involvement in an accident/injury event.

In order to grasp the magnitude of the accident problem on Ontario farms, one must examine two very different sets of data: mortality and morbidity. Mortality data are, of course, "hard data" and relatively easy to collect and examine. There are, after all, relatively few accidental deaths on farms, and Coroners Office and vital statistics data can be filtered to produce a reasonably accurate picture. However, it is axiomatic in trauma surgery that for every fatality there are three permanent and total disabilities such as a brain or spinal cord injury, and 10 permanent partial disabilities, such as amputation or loss of an eye. This, of course, says nothing about a temporary disability such as a broken wrist or infected cut on the foot. These data are obviously "softer", and much more difficult to collect and examine, and are very numerous indeed.

Examination of death certificate data can lead to accident mortality rates for population sub groups such as farmers. This

rate can be compared with the expected accidental death rate in the population as a whole, to construct a proportional mortality ratio (PMR). For example, Gallagher (1984) in a study in British Columbia found that the PMR for farmers for all accidental deaths was significantly elevated at 129 while the PMR for cardiovascular disease was only 89. In California, Carlson (1978) this was taken one step further. Separate PMRs were calculated for farm labourers and for farm owners and managers. The PMR for labourers was startlingly high at 315, and was moderately elevated at 146 for farm owners and managers. A later study in California, Stubbs (1984) indicated that the PMR for all accidents for labourers was still significantly elevated, but that there was no increase in mortality for farm owners and managers. Similarly a study in Iowa, Burmeister (1982) also showed excessive mortality in work-related accidents. Unfortunately very few states and provinces calculate occupation specific mortality ratios, and accordingly these data are rather thin.

A more useful way of examining mortality data is to look at a series of deaths case by case. The Farm Safety Association in Guelph, Ontario collects data on all fatal accidents occuring on farms in Ontario. These data are reliable and have been remarkably stable over the last decade. According to the FSA, between 1975 and 1983, 407 people died accidentally on Ontario farms; an average of 45 deaths a year. When analyzed by cause, the tractor is identified as the agent of death in over one half of the cases. Typically, the tractor rolls over sideways or flips over backwards, crushing the driver. Sometimes a passenger, often a child, falls off and is run over. The power take-off unit, if unshielded, can be particularly vicious as well. The tractor is identified as the most common vector in similar reviews from Georgia, Smith (1983) Texas, Jackson (1983), New South Wales, Australia, Whealing (1981). At the 9th World Congress for the Prevention of Occupational Accidents and Diseases, Freeman (1980) it was reported that tractor fatalities in Europe were lowest in Sweden, Denmark, and West Germany. These countries have legislation which mandates rollover protection on all tractors, both old and new. In fact, standards for rollover protection are now becoming widespread throughout Europe. In Wisconsin, Karlson

(1979) felt that voluntary standards had failed, and thus legislation was necessary. She presented data which showed that tractor deaths in Wisconsin had increased on a per capita basis, although she omitted to mention that the number of tractors in use was also increasing.

Other farm deaths have been related to machinery such as harvesting equipment and augers. Less common causes of accidental death are also reported. These include the use of other vehicles on the farm, fatalities linked to drowning and suffocation, poisonous gases, being hit by falling objects, and electrocution. However, these data do not address accidents which are farm related but in fact occur off the farm. This would include accidents involving farm machinery on public roads. In addition, deaths related to the storage or processing of farm produce are not addressed in this manner. For example, the grain elevators that dot the prairie countryside are well known to be hazards for serious explosions. In fact, in a one month period between December 21st 1977 and January 21st 1978, seven of these grain elevators in the U.S. exploded, killing 62 people and injuring many more. One of these structures was a large, brand new elevator in Galveston, Texas. Regulations for ventilation of grain elevators and the reduction of static electricity have since been introduced in many states.

Morbidity data from farm accidents are much more difficult to collect and analyze. Centralized data collection simply does not exist. One must furthermore carefully define "disability" for purposes of analysis. The Workers' Compensation Board collects data regarding "lost time injuries" on farms. However, the WCB only extends coverage to the one third of Ontario farms which have paid employees, and then only to the employees themselves; and not to the employing farmer or his family.

The trauma literature is scattered with exotic case reports affecting such widely dispersed groups as cherry pickers in Switzerland (Mauser 1981) and manure removers in Denmark (Tyge Lind 1982). Closer to home, fracture of the sternum may become

known as "hay balers fracture", based on a series of two such cases in Manitoba (Mayba 1984). However, such reports do little to help us understand the more common hazards facing Ontario farmers.

One method of reporting injuries is the hospital based case series method. By this method, all injuries serious enough to be admitted to hospital are reported and patterns within the series can be sought. If the hospital is in the centre of a rural farming area, and the referral patterns are well established, then some estimation of the magnitude of serious injury can be made. However, in general, such series are useful mainly to point out a particular hazard, such as a certain piece of machinery.

For example, Simpson (1984) looked at 44 hospital admissions in 1980 in Saskatoon. All patients were the victims of farm machinery accidents. Again, the tractor was the most common agent of injury. Injuries resulting from power take-offs (amputations) and augers (crush injuries and compound fractures) were found to be particularly disabling. In addition, most of the injuries were felt to be preventable if safety features such as rollover protection and safety shielding had been in place.

A particular piece of machinery may be the subject of a report. For example, the power take-off was the subject of separate reports from the Mayo Clinic, McElfresh (1973) and Hershey, Pennsylvania, Kalenak (1978). A power take-off is an extension of the drive shaft of a motorized vehicle such as a tractor, and provides the major source of power for many farm implements such as corn pickers, elevators, and blowers. It may be exposed during the period of engaging the two vehicles and perhaps even while the vehicles are in operation. Shielding is usually provided but frequently is inadequate or removed for repairs. An impressive array of compound fractures, traumatic amputations, severe deep lacerations, major neurovascular injury, and serious infections was presented. Similarly, the corn picker was singled out as an agent of destruction in separate reports from Iowa, Melvin (1972) and again from the Mayo Clinic, Campbell

(1979). This machine can inflict mutilating wounds to the hand, causing traumatic contaminated fracture dislocations and amputations, usually to the dominant hand. In the Mayo Clinic Series, the average length of disability was 135 days and 89% of patients experienced some permanent impairment of hand function.

The grain auger has also been singled out as a particularly dangerous instrument. Reports from Manitoba (Grogono 1973) and (Letts 1978) and from Illinois (Beatty 1982) document once again the severe nature of traumatic fracture dislocation and amputations associated with the auger. Once again, a plea for a better design of safety shields was made. The report from Manitoba (Letts 1978) was particularly disturbing because it related to injuries sustained by 23 children over a 6 year period. Roughly half of all traumatic amputation of childrens' limbs in Manitoba seen at the child amputee clinic in Winnipeg relate to accidents with the grain auger.

Farm injury to children is surely nothing new. However, one alarming development has been the increasing number of motorcycle accidents sustained by young children. These are usually on the all terrain type of trail bike becoming so popular today. While children cannot operate these vehicles on the public roads, there are absolutely no restrictions to their use by children on private property. In 1984, Yong-Hing presented data to the Royal College of Surgeons regarding 51 children who had been admitted to the University Hospital in Saskatoon with motorcycle injuries. Well over half of these injuries occured on farms. Similarly, there are no restrictions regarding the use of the tractor by a child while on the family farm. Often, by the age of 13 or 14, a child will have learned these skills but be lacking in the emotional discipline or judgement required to use them properly.

The case series type of report serves well to highlight a particular hazard, but does little to assess the overall impact of farm accidents. An extension of the case series type of report is the survey report which is done by administering a questionnaire to all patients who satisfy certain criteria, such

as being admitted to a hospital. Such surveys were done in Alberta (Howell 1973), Saskatchewan (Hill 1975), and here in Ontario (Sullivan 1979). The purpose of the surveys was to assess the blame, or at least the level of preventability of the event. Such factors as emotional maturity, attitudes towards safety and experience with the machinery are analyzed but because of the lack of control subjects or the lack of exposure data, a true understanding of the causes could not be advanced. The Saskatchewan study in particular had problems defining a farm accident, and eventually ended up surveying only those who were actually admitted to hospital with their injuries.

On a more global scale, in order to estimate the number of people injured, the number of man hours lost, and the economic losses, a more costly survey of large numbers of farms is required. This type of survey must be prospective or cohort analytic in type. Certainly the pioneer study in this field was the Ontario Farm Accident Survey which was undertaken from March 1959 to February 1960. The entire farm population of Ontario was followed for this period. The results of the study were truly astounding, in that 293 farm people were killed, 336 were permanently disabled, and 5,868 had some less severe form of injury. The costs of medical expenses and property damage were extensive. A similar study was carried out by the Canadian Chamber of Commerce in its 1964 Farm Safety Survey. A random sample of 49,000 persons living and working on various types of farms across Canada was chosen and followed. The results showed that one member of every fourth Canadian farm family was involved in an accident that year, that one half of these accidents required hospitalization, and that 2% of these accidents were fatal. These two cohort style studies remain unique to the Canadian scene. However, a number of U.S.A. studies have taken place in the same manner. In Michigan (Pfister 1969) it was found that there were 13.1 accidents for every 100 farms, or one accident for every 7.6 farms in that year. Similarly in Iowa (Hull 1977) a cohort study identified one accident for every 5.6 farms. These accidents were linked to youth and inexperience. Again, the tractor, other farm machinery, ladders and animals were the main contributing factors.

The Workers' Compensation Board in Ontario reports that in 1983 there were 2,812 injuries to paid employees on 25,533 farms; roughly one injury for every 9 participating farms. The weighted average claim was $3,352.00, which represents a total outlay of 9.4 million dollars to these workers. However, there are no data to estimate the amount of lost time experienced by the larger number of employer or self-account farmers or their families.

After examining this information, several things become clear:

1. The tractor is the main agent of death and severe disability on Ontario farms. Mandatory installation of rollover protection devices on both new and old tractors would greatly reduce the number of fatalities. These devices are now mandatory in many European countries.

2. Mandatory shielding of power take-off units and of machinery such as the auger would greatly reduce the number and severity of injuries that these instruments are capable of producing.

3. Inexperience and immaturity are a factor in accident etiology. Educational programs such as those promoted by the Farm Safety Association, although impossible to evaluate objectively, can only be encouraged in the strongest possible terms.

4. Accidents to children occur at an alarming rate. These children are often operating dangerous machinery or vehicles.

5. The overall burden of non-fatal injuries on Ontario farms is impossible to assess. Every year there is probably one accident for every 5 to 7 farms. If more accurate data are desired, then a comprehensive cohort study is required.

## Noise

Thelin et al (1983) measured the hearing of 161 male farmers and 75 male nonfarmers at the 1979 Missouri Farmers Association Agri-Fair and compared it with the hearing of 129 office workers

from central Missouri. Fixed-level screening tests were conducted in both ears at three stimulus frequencies: 1000 and 2000 hertz at 20 decibels hearing level and 4000 hertz at 25 decibels hearing level. Audiometers were calibrated in accordance with the ANSI - 1969 standard. The results show that farmers are at risk for hearing loss at 2000 and 4000 hertz when compared with office workers. The prevalence of hearing loss was greater for farmers at both frequencies in every decade age group from 25 to 64 years. Using screening failure at 2000 and 4000 hertz in both ears as a criterion for a loss that would affect communication ability, they found that the failure rate was 16.8 percent for farmers and 6.2 percent for office workers. As other investigators have found, the prevalence of high-frequency hearing loss in male nonfarmers who associate with farmers was nearly as great as for farmers.

Sullivan et al (1981) presented the results of a year-long study of the noise environment of agricultural workers on Nebraska farms. The farms which were chosen to participate in this study were selected on the basis of:

Willingness to cooperate,
Type of farming operation,
Number of employees,
Kinds of equipment used, and
Age of equipment used.

After meeting a number of farmers, six farms with more than 60 employees were selected with field lot production, ranching and confined feedlot operations. Equipment was characterized by the sound it produced under three load conditions. In each load condition the sound level and noise exposure was established for all high noise units. The three load conditions were:

Light Load - Low engine RPM. Doors and windows closed on tractors with cabs. Low noise produced during chores, cattle feeding and light hauling operations.

Medium Load - Medium engine RPM. Doors and windows open or closed as appropriate. Moderate noise produced during hauling, loading and intermittent full load operations.

Heavy Load - Full engine RPM. Highest noise produced under operating conditions. Most field work, disking, plowing and combining were in this categor.

Work records maintained by the employers and noise dosimeter data were used to calculate daily noise exposures. The daily exposures then were used to determine the monthly and yearly exposures.

There were a total of 495 worker months in the study. In only 77 of these worker months was the exposure above 100% of allowable. The monthly occurrence of moderate and high risk exposures for all employees peak in June through September.

Twenty-six employees experienced at least one month when the noise exposure limit was exceeded. The 12 employees exposed to more than the low risk category accounted for 49 of the months of over-exposure were attributable to 14 employees receiving at most three months of over-exposure during the year.

A total of 10,885 days were worked by all employees. On 1,834 days, 17%, the daily exposure limit was exceeded. The average day length was 9.3 hours and working days in excess of 12 hours were common.

The noise exposure pattern of the agricultural industry is unlike that of factory type industries. In general, the noise generated on farms is concentrated in the summer months. Different seasonal noise exposure patterns are produced for the different types of farms. Ranches typically have high noise periods during hay harvest. Farms with feedlots that harvest ensilage have high noise periods in the spring during field work and in August and September during forage harvesting. Similarly, cash grain farms have high noise periods during spring field work and again in September and October during grain harvesting.

The only accurate way to define noise exposures of employees is to determine the annual work schedule on the farm and then relate this schedule to the sound levels of the various agricultural operations. This information can then be assigned to the individuals performing each operation to estimate the noise exposure they will receive daily, monthly, or annually.

Much of the equipment used on farms today still produces sound levels above 85 dB(A). All of this equipment has the potential for causing daily excess noise exposure for an employee. The equipment units most likely to produce annual, monthly, or daily excess exposures to noise are:

1. Tractors without cabs, or with cabs lacking sound

suppression insulation.

2. Forage choppers and combines, and

3. All self-propelled equipment.

Another area for concern is the use of farm equipment more than eight hours per day.

McCarthy (1981) commented that operators of tractors and other farm machinery are receiving noise doses exceeding the 90 dB/eight hour limit set by the Occupational Safety and Health Administration. McCarthy said tractors emitted noise levels averaging between 93 and 100dB. "Farmers have a higher hearing loss than other professions, and the cause is daily exposure to the noise of farm equipment." Sample noise level readings from other machines indicated that compressors run all day at noise levels of 100 dB; metal drills can reach noise levels of 110 dB when only turned on and not actually drilling; and the process of using a saw to cut bushes can produce noise levels of 103 dB, according to McCarthy. She said that farm workers who must follow picking machines are subjected to noise exposures that are "dangerously high" because they do not use hearing protection. High frequency hearing loss among farmers can be reduced by insulating tractor cabs using hearing protectors, repairing tractor mufflers, and conducting audiogram testing at the beginning of employment and at yearly intervals, she noted. Workers in agriculture and construction were exempted from new rules governing occupational hearing conservation programs issued by OSHA.

Scamoni et al (1981) noted that the number of persons exposed to noise in the agriculture of the German Democratic Republic increased considerably in the last years. Agrotechnicians at 43% of the total represented the largest group of workers affected by noise. Most of the noise has its source in agricultural machines and tractors. The statistics of occupational diseases reveal that the range of agricultural, forest, and food economy had the greatest incidence of noise-induced loss of hearing in all branches of political economy in 1979. Conclusions for reducing noise induced hearing loss are

contained in the plan to fight against occupational diseases in agricultural, forestry, and food economy.

Talamo (1979) reported that the ability of tractor drivers to perceive tonal signals has been measured in a range of tractor and cab noise environments. These include: a tractor with a simple open safety frame; a tractor with an experimental noise excluding cab; a noisy, partially enclosed cab with a rigidly attached safety frame and sheet metal cladding; and the latter with the driver wearing hearing protectors. The effects of cab attenuation and noise masking are shown separately and in combination. Both noise-reducing cabs and hearing protectors are shown to have relatively minor effects on tonal signal detectability. The effect of the same working environments on the ability of drivers to detect shouted warnings and to identify their direction of origin are then compared. The low probability of a driver hearing a warning shouted from distances greater than three metres is demonstrated. In this condition hearing protectors are shown to increase detectability slightly but to increase directional errors.

Dekker et al (1978) reported that the constantly advancing mechanization in agriculture is a threat to good hearing function. An investigation among tractor drivers in The Netherlands showed that: - the thresholds of audibility of tractor drivers working in agriculture for more than 10 years correlate with those of employees in industry exposed as many years to a constant noise of 90 dB(A); at least this holds for the changes in the threshold of audibility at frequencies up to 4000 Hz; the shifts at 6000 Hz and 8000 Hz found in the tractor driving population correspond with those caused by sound levels of 100 dB(A).

Skvaril and Dennis (1975) in a report of the Prairie Institute of Environmental Health describe the cumulative affects of farm machinery noise on a population of Saskatchewan farmers. The great majority of the 1,376 farmers examined during the survey had had no other occupation so that the noise exposure which they had incurred was confined to noise sources on the

farm. The assessment of individual farm noise exposure is complicated not only by changes in farming techniques but by changes in farm size and by changes in farming practice from mixed farming to grain farming, where noise exposure is mainly confined to a number of months of intense activity from May to October. These differences, compared with the relatively constant noise exposure of specific industrial populations for regular periods of daily exposure, make the prediction of farm noise effects based on data accumulated from industrial noise exposure difficult. This is compounded by the early involvement of young farmers with tractors so that significant noise exposure can occur before the age of 18.

In male farmers cases of noise-induced high frequency hearing loss were found in all age groups assessed. Cases of hearing loss likely to impair the ability to discriminate between sounds and communication in the presence of background noise, were found in the 25-34 and subsequent age groups. A significant decrease in hearing acuity at low frequencies which could impair the hearing of ordinary conversation even in the absence of background noise was displayed by more than 10% of farmers aged 45-54 and by more than 25% aged 55-64; this percentage rose to more than 50% in farmers 65 years and older. The hearing acuity of farmers who shot was poorer than farmers of a corresponding age who did not shoot. The hearing acuity of farmers aged 25 and older was poorer in the left than the right ear for reasons suggested in the report.

In female farmers no evidence of noise-induced damage to hearing was found. The evidence suggests that women who farm are not exposed to farm machinery noise to an extent that presents a significant hazard to hearing.

The high incidence of high frequency hearing loss in the young male farming population as compared to a comparative population minimally exposed to noise confirms that exposure to farm machinery noise presents a particular hazard to the hearing of the young unprotected farm population. Comparable hazardous farm noise exposure before the age of 18, i.e. in the maturing period of life, was found to have caused a greater hearing loss

than the same noise exposure after the age of 18.

The report recommends that a strong information and educational program be introduced in rural schools to prevent adverse health effects amongst young farmers and that further research be carried out to define and reduce the increasing risk of noise-induced hearing loss in the young.

Siesweerda (1978) reported on deafness caused by tractor noise. In the agricultural sector increasing mechanisation means a burden of noise for the farmer and his co-workers. Therefore a study of the nature and spread of hearing loss among tractor drivers was undertaken in the years 1975 - 1978 at Leens, Harich and Franeker. The results thereof are disturbing.

From the study conducted at Leens, it appears that hearing loss in tractor drivers of approximately the same age occurs when they have to work year-round with a noise of 90 dB(A). Severe hearing loss in the agricultural field should not be differentiated from that which is regulated in the traditionally noisy occupational sectors. In the Franeker study, results showed that tractor noise had a more damaging effect upon the older drivers (more than 25 years) than upon the younger ones. In the study at Leens the exposure varied from 300 to 1500 hours annually.

May (1971) commented on the extent to which physical and mental health of farm machinery and equipment operators is adversely affected by unsatisfactory environmental and design features.

Seidel and Troster (1970) reported that in 1969, 60 tractor-drivers were medically examined and interviewed. Before, noise- and vibration measurements were performed at various types of tractors. It turned out that the sound level of almost all types of tractors, even that of the newly developed ZT 300, was above the admissible noise evaluation curve N 85. At the vibration measurements on the bottom of the vehicle the "concentration" values were within a range in which - according to Dieckmann - a "ride in vehicles for a prolonged period" is admissible. Upon medical examination, it was revealed that the pain on the

vertebral column ranks foremost amongst the farmers' concerns. In most cases the tractor drivers described that this pain is released by the work on the tractor or intensified thereby. This also applies to the stomach pain stated by the tractor drivers. The cause might be a vibration mixture which - in addition to the vibrations of the vehicle floor, is composed of motor vibrations, the uneven condition of the road and of the spring-suspension of the tractor. As far as the stomach pain is concerned, both vibrations and noise play an important role. Twelve tractor drivers complained about buzzing in the ear and a sensation of deafness after work. When evaluating the audiograms, the authors ascertained that the loss of hearing at the frequency of 400 Hz increases along with the advancing vocational years. The difference is largest between the vocational year groups 5-10 and above 10 years. Probably, the auditive organ of the tractor-drivers is endangered by the exposure to noise.

Simpson and Deshayes (1969) reported on a tractor noise study by the University of Nebraska that shows that virtually all tractors presently in use in the United States produce noise in excess of the 85 decibel ear-damaging level. The Division of Environmental Health and Safety, University Health Services, University of Nebraska, with the help of a consulting audiologist, conducted a three-year survey of hearing acuity among employees working with farm equipment at the university experimental stations. One hundred forty six men were tested. Forty were tested three times at one-year intervals. Ages ranged from 18 to 64 and working conditions varied from noise exposure 2-3 hours a day to 5-8 hours a day. All audiometric evaluations were made with a Bruel and Kjaer (B&K) precision sound level meter with octave filter set ranging from 31.5 c.p.s. to 31,500 c.p.s. Results of the survey show that hearing acuity ranged from normal (average 10 db in all frequencies tested) to moderate-severe hearing loss. At the beginning of this survey, acoustical ear plugs were furnished for those employees at the experiment stations working with farm equipment. After the third survey was completed, changes in each man's hearing were studied. Figure 4 shows results of those who did not wear acoustical ear plugs, those who wore plugs only around noise which "hurts" their

ears while working (feed grinders, driers, hammer mills) but not around tractors, combines and corn pickers; and those who wore ear plugs during the entire working day.

In an Editorial in Industrial Hygiene News (1968) it was reported that sound pressure levels which are capable of producing permanent hearing loss are generated by a major portion of the power equipment used by the modern farmer. In a tractor noise level study the noise level generated by 55 farm tractors and 18 other types of farm equipment was determined. A special microphone was mounted near the tractor operator's ear, and noise level readings were recorded on a precision sound level meter. The over-all and octave band sound pressure levels were measured at 100% tractor load, 75% tractor load, and 50% tractor load, based on pre-determined horsepower of each tractor. All types of farm tractors were studied and 18 other types of farm equipment, including combines, corn pickers, elevators, etc. The lowest over-all sound pressure level for tractors was 97 db and the highest was 114 db, as compared with the commonly accepted level of 85 db as the upper limit of sound pressure level to which a person may be exposed over an extended period of time without appreciable loss of hearing. Results from other farm equipment gave an over-all sound pressure level from 90 db on an electric roller mill to 113.5 db on a reciprocal blade power saw.

Jones and Oser (1968) recorded noise levels during performance tests conducted at the College of Agriculture, University of Nebraska, on 58 new tractors and 20 other types of farm machinery. They were of such intensity, duration, and distribution as to indicate a potential permanent noise-induced hearing loss to the agricultural worker. Of the tractors tested at 75% of full load, 90% exceeded the recommended 85-dB average level for the three octave bands centered at 500, 1000 and 2000 cps. Of the 20 pieces of special farm equipment tested, 65% exceeded this recommended level. The average overall sound pressure level for all models, types, and operator positions was 103.5 dB.

Lierle et al (1958) commented on the effect of tractor noise

on the auditory sensitivity of tractor operators. During the practice of otolaryngology for the past several years in a rural area, a sufficient number of farmers with 4000 cycle dips have been noticed to attract special attention. In some instances the ear history and physical examination have been negative except for the probability of tractor-noise-induced hearing loss. However, it also has been observed that certain farmer patients who drive tractors have been seen with normal hearing.

Tomlinson (1971) reported on estimation and reduction of risk to hearing: the background and a case study. He suggests that for noise exposure varying in both level and duration, current noise criteria are inadequate but, by adapting methods presently available, an equivalent continuous level can be calculated from which the risk to hearing can be assessed. The predicted effects on hearing compare favourably with measured values. These methods are used to predict an 'acceptable' noise limit for the variable noise environment on the agricultural tractor. He outlines methods of noise reduction for the tractor along with other approaches to hearing preservation.

Stayner (1978) reported on a survey of tractor drivers' hearing, 1976 - Report to Health and Safety Executive. Hearing levels of 166 tractor drivers chosen from amongst those attending two major agricultural shows were measured. The noise exposure histories of 120 of these subjects were estimated using a questionnaire together with the results of a noise measurement survey, whence the noise-induced hearing loss of each subject was calculated. The measured hearing levels indicated losses much greater than those calculated, despite efforts to screen the subjects and to include noise exposure from all other activities as well as from tractor driving.

Stayner (1975) reported on noise exposure of tractor drivers Noise levels on tractors at the time this study was made were well above recommended limits for hearing conservation. The average noise level was 94.6 dBA with a maximum of 103.7 dBA, and the average equivalent continuous sound level was only slightly

lower at 93 dBA, with a maximum of 101.4 dBA. Tracklaying tractors were about 2 dBA noisier than wheeled tractors, but there was no significant difference in overall levels between 2 and 4 wheeled drive tractors. Noise levels on combine harvesters were 3 or 4 dBA lower than on tractors, but at that time only 15% of the machines were fitted with cabs, which tended to increse noise levels by 2-3 dBA. Noise levels on other self-propelled machines were similar to those on tractors. The results show great variability because of the wide range of machines and operating conditions encountered. Factors which were found to have a large effect on noise level include:

- operating speed (10 dBA/doubling of speed for individual models
- tractor model/cab design (82 dBA to 101 dBA)
- task or implement (88 dBA to 99 dBA)

Less important were:

- tractor power (rated)
- tractor configuration (2-4 wheel drive or tracklaying)
- number of doors or windows open

The relationship between noise levels under working conditions and noise levels under test conditions is more complex than what had to be assumed in 1970. Then the median field level was observed to be 9 dBA below the median test level, and in setting the test limit, this was conservatively reduced to 5 dBA. The evidence is that for lower noise levels the difference between field and test conditions is reduced, and the probability of the test level being exceeded increases. This will be in proper perspective when values for total annual exposure have been calculated. However, it must be remembered that it was hoped that the test limit of 90 dBA would produce an average field level of 85 dBA and so protect 95% of the tractor driving population from noise induced hearing loss.

Stone (1967) carried out a preliminary survey of occupational deafness and the hearing acuity of employees in the agricultural industry. The limited results from this part of the survey provide clear evidence of the need for hearing conservation methods to be adopted. The most effective method of reducing the noise hazard of existing vehicles would be to

provide individual protection for the drivers. Ear muffs give the greatest protection, usually 30 dB, attenuation for all frequencies, but they are not always acceptable and are relatively expensive. The attenuation characteristics of insert defenders vary greatly and a type must be chosen which will reduce the individual noise levels to within the safety limits. The noise level inside a vehicle cab can be reduced by lining the cab with sound absorptive material, or by reducing the noise-generating vibration of the cab structure. However, while the amount of noise reduction achieved may produce a more pleasant environment for the driver, care must be taken to ensure that the noise level has, in fact, been reduced sufficiently for hearing conservation. Certain features of vehicle design could be modified to reduce the hazard to hearing. This is undoubtedly the most satisfactory long-term approach to noise control.

## Vibration

Davis (1984) obtained formulae for two standard vibration signals for tractor seat tests by statistical analysis of the time series of sample displacements used to define the signals. Such formulae could be adoped as more compact and less restrictive choices for the definitions of the signals. One of the research objectives pursued at the NIAE is to improve the ride characteristics of tractors in order to increase driver comfort and potential working speed.

Kasamatsu et al (1981) discussed vibration hazards which arise after exposure to mechanical vibration comprise various types of disorders, the most common of which are peripheral circulatory disturbances. It is now well recognized that aging affects all organ systems of the human body. This study was therefore performed to assess the effects of aging on finger skin temperature and on hyperemia time after pressing the nail, both of which reflect peripheral circulatory functions. The subjects were 88 farmers and 86 chain saw operators ranging in age from 30 to 69 years, and 27 healthy persons aged 21 and 37 years as

controls. Data were evaluated before and after cold water immersion tests in which the hand was immersed in 10 deg C water for 10 minutes. The results obtained were as follows:

(1) Before the test, skin temperature was negatively correlated with age, and hyperemia time was positively correlated with age in both farmers and chain saw operators but not in the case of the control subjects.

(2) The skin temperature became lower, and hyperemia time grew longer with advancing age in both farmers and chain saw operators before and after the immersion test.

In comparison of the average skin temperature and hyperemia time between farmers and chain saw operators classified by age, the average skin temperature in chain saw operators was significantly lower than that in farmers, and the average hyperemia time in chain saw operators was significantly longer than that in farmers of every age group after the immersion test. The results suggest that we should take age-related changes into consideration to some degree when we evaluate the finger skin temperature and hyperemia time in diagnosing peripheral circulatory disturbances.

Kauko Turtiainen (1974) reported on a study during limbing, the highest mean vibratory acceleration in the front handle of saws without shock absorbers was 77.0 $m/sec^2$ in the wrist direction, 117.0 $m/sec^2$ in the guide bar direction, and 96.5 $m/sec^2$ in the axial direction. In chain saws with shock absorbers, the corresponding figures were 32.5 $m/sec^2$ in the wrist direction, 45.0 $m/sec^2$, 45.0 $m/sec^2$ in the guide bar direction, and 30.5 $m/sec^2$ in the axial direction. The corresponding figures for the rear handles of saws without shock absorbers were: 93.0 $m/sec^2$ in the wrist direction, 81.0 $m/sec^2$ in the guide bar direction, and 110 $m/sec^2$ in the axial direction; and in saws equipped with shock absorbers, 37.7 $m/sec^2$ in the wrist direction, 41.9 $m/sec^2$ in the guide bar direction, and 44.2 $m/sec^2$ in the axial direction. In saws with shock absorbers the vibratory accelerations are generally the same in both handles, and the difference between limbing and bucking is very small. On the average, vibratory accelerations in saws without shock absorbers are 2.5 times greater than those in saws with shock absorbers

and, in extreme cases, can be 8 to 16 times greater. In all saws the vibration is generally greater in limbing than in bucking. Rubber shock absorbers should be changed after approximately 200 hours of use, because their absorbing effect is reduced.

Hellstrom and Andersen (1972) offered a free medical examination with compensation for lost earnings to the forest workers in three areas of eastern Norway. Sixty-six percent attended (413 workers, of whom 296 used chain saws). The prevalence of Raynaud's phenomenon was 47% in chain saw operators, 14% in forest workers not exposed to vibration, and 9% in 302 indoor workers not exposed to vibration. The high prevalence of RP in chain saw operators was attributed to a traumatic vasospastic disease (TVD). The average time of latency was eight years. The standard symptoms of TVD were attacks of blanching and numbness. Cyanosis and pain occurred rarely. In subsamples, measurements of tactile two-point discrimination and maximal isometric muscle strength (hand grip and finger pressure) as well as x-ray examinations of the wrists and the hands give no evidence of vibration injury to peripheral nerves, muscles, bones, or joints.

Huang and Suggs (1967) reviewed vibration studies of tractor operators and studied field working conditions in order to determine the vibrational characteristics of farm tractors. Also to determine, by means of laboratory simulation, the physiological response and performance deterioration of human subjects exposed to two temperatures and to a range of sinusoidal vibration in the vertical, longitudinal, and transverse directions for the most critical frequencies found in the field observations. Of the field operations studied, disking plowed ground gave the most severe vibration to a tractor operator in vertical, longitudinal, and transverse directions. Of these three directions, the vertical vibration resulted in the highest acceleration and frequency distribution ranges. Environmental temperatures at 60 F and 90 F had little effect on the response of the subjects to the imposed vertical vibration. There was, however, the expected heart-rate increase with temperature and a

slight decrease in oxygen consumption with increases in temperature. Higher vibration in the vertical and longitudinal directions resulted in an increased ventilation rate. In transverse vibration, the tracking error became significantly larger for higher accelerations. The heart rate and ventilation rates were high in the neighborhood of 1 g acceleration, but they were slightly lower at 1.5 g and 2 g for transverse vibration. Although the vertical vibration had the most significant effect on man, the physiological and performance effects due to the longitudinal and transverse vibration should not be ignored. The vibration transmitted through the steering wheel has a significant effect on ventilation rate and body acceleration. The ventilation rate was significantly higher for the hands-on position for both longitudinal and transverse vibration. The waist acceleration was considerably larger than the chest acceleration for both the hands-on and hands-off positions. For longitudinal acceleration both waist and chest accelerations tended to increase as the imposed acceleration was increased. However, they had a tendency to decrease at a higher imposed acceleration for transverse vibration.

Matthews (1968) reported some measurements of vibration encountered by operators on agricultural machinery. Considerable vibration is induced in the structure of machinery by either the power unit or the moving parts of the machine. This vibration is frequently transmitted to the body or limbs of the operator where they are in contact with the machine - either on the seat, foot platforms, or hand or foot-operated controls. If excessive, the vibration may result in undue discomfort of the operator or in a risk of clinical trauma. The important components of vibration are generally in the medium or higher frequency range. Lower frequency vibration, normally arising from vehicle travel, has been treated as a separate problem. The upper limit of the range considered is mainly defined by the speeds of operation of the combustion engines incorporated from the measurements made it became clear that the frequency range 20-200Hz is the important one.

## Ergonomics

Sjoflot (1984) reported that a five year research program is going on in Norway in order to coordinate all research activities and create good professional conditions in the field of ergonomics in agriculture and forestry. The programme consists of 9 different projects at 7 institutions and is responsible for some teaching and special information service. The steering committee represents users of results. The projects briefly described are on forestry and farm work and health, safety and ergonomics in farm buildings and on farm tractors in agriculture and forestry, spraying of chemicals, psycho-social factors in family farm work, women and children situation on farms, occupational health services for the rural population. The organization of the programme, the experiences so far and a brief review of results from some projects are given.

Ergonomics and farm machinery were reviewed by Matthews (1983). The application of ergonomics investigation and of good ergonomics principles, to the design of equipment may be justified in two completely separate ways. Firstly, it is clearly important that the occupational health of the worker using the equipment is not detrimentally affected by characteristics of the equipment, such as the need to adopt awkward postures, damaging environments or accident hazards. Apart from health and safety considerations, however, there is considerable evidence of the correlation between good ergonomics practice and the efficient use of the equipment. Early ergonomics research showed how the posture of operators on transplanters could affect through their ability to work efficiently, the number of healthy plants ultimately grown. More recently studies of noise level on tractors have indicated a relationship between the intensity of noise at the operator's ear and the speed at which the tractor is set to work. Evidence that those drivers who have noisier vehicles are inclined to choose a lower engine speed to maintain a reasonably comfortable noise level and thereby carry out the work with the tractor at a lower forward speed and hence at a lower work rate.

It appears probable that ergonomics design changes may continue to be the most obvious evolution of tractors. The improvement of ride comfort appears to be of high priority and attempts to improve postures could also be valuable. It has been realized for some time that it would be an extremely valuable research tool to be able to measure reliably the extent of fatigue of a driver at the end of his day's work or even at periods during the work. This could be useful to assess the benefits of many of the changes which can be made.

In reducing the driver's efforts or improving his environment it is important that he is left with a sufficiently challenging and interesting task. The man and the machine each exhibit well-known and catalogued characteristics which to a large extent complement one another and it is important that in future engineering of tractors this fact is borne in mind.

Bottoms (1983) describes an experiment designed to test an index of tracking difficulty for agricultural driving tasks as an analogy to Pitts' Index of Movement Difficulty. The proposed index is defined as a function of the ratio of vehicle width to tolerance available. The results suggest that while the original proposal had some merit,a better index may be one in which the dominant term is the reciprocal of the maximum heading angle error.

Pulbere et al (1982) reported the results of the clinico-roentgenographic diagnosis and treatment of 1026 agricultural workers with osteochondrosis of the spine. Osteochondrosis of the spine is more frequently observed in the collective farmers and state farm workers working on the plantations of sugar beet and tobacco, mechanics and drivers of autotransport, which is connected with the character of their work. In subjects over 40 years of age the diffused osteochondrosis was often combined with arthroses deformans of the knee, hip, shoulder joints. The complex, conservative therapy in conditions of orthopaedic stationary gives 82% of positive results. The operative treatment is indicated in ineffectiveness of the conservative

therapy.

Miller (1982) investigated whether the protective equipment tractor drivers wear when spraying crops might itself create a hazard. He measured the heat stress of a tractor driver over a 2-1/2 hour period as he continued to wear his non-absorbent plastic type protective clothing while sitting inside a tractor cab after mixing the chemicals. What he found was alarming because even on a moderately warm day heat exhaustion sufficient to impair judgement was likely to occur. The cab of a tractor was fitted with equipment to record environmental conditions. A driver's skin temperature was monitored at 11 points and deep body temperature was measured by ear probes. During 2-1/2 hours of driving the deep body temperature rose from 37.8 deg C to a maximum of 39.4 deg C - a level thought too high for bodily physiological actions and at which responsible behaviour might be affected. Skin temperature rose to 38.4 deg C which was thought to be too high for comfort. It is concluded that the practice of driving tractors on even moderately warm days while wearing a plastic suit is dangerous when the operator needs to exercise skills.

Schrottmaier (1982) presents data on the control requirements of 64 different types of machine and indicates that many controls must be operated from the tractor seat. An examination of the workspace envelope around the seats of tractors fitted with cabs demonstrates the practical problems that arise from the operation of tractor-mounted or trailed equipment. The evolution from protective frames, which are mandatory in many countries, to protective cabs has increased the quality of working conditions. The ability to handle other machines and equipment attached to the tractor has, however, deteriorated with the introduction of the cab.

Sjoflot (1982) presents the results of a national survey of Norwegian farmers. The survey was undertaken because of the lack of information on the farmers' own opinions of tractors, tractor operation and working environment; of the age, condition and time in use of tractors and different equipment; of the farmer's and tractor driver's health conditions and their opinions on recent

ergonomics developments. The survey results provide the basis for deciding future research and development and also to assign priorities.

Pheasant and Harris (1982) comment on human strength in the operation of tractor pedals. Tractors require more pedals than road vehicles: the placement of these pedals presents a complex task for the designer. Since pedal position is an important determinant of the posture of a vehicle driver's pelvis and spine, it is essential that this problem be carefully considered. (The tractor driver's spine is already potentially at risk through high vibration levels and the need to twist in the seat while monitoring tools at the rear of the vehicle.) Anecdotal evidence suggests that an increasing number of women wish to drive tractors. The consequent increase in the variability of the user population will exacerbate existing design problems; pedal resistance must be within the strength capability of the weakest female driver but must not be so low as to make control difficult for a heavy footed male. The ergonomic literature concerning human strength in the operation of pedals, although extensive, is not entirely adequate for the tractor designer. Studies have either been conducted on subjects in specific postures, defined in anatomical terms which are not easy to relate to workspace design problems, or else have been ad hoc investigations of single pedal locations in specific vehicles. The present study is aimed at elucidating the biomechanical factors which influence human strength in the operation of a pedal. A better fundamental understanding of these problems would allow better advice to be given to designers. The following variables were investigated: (a) horizontal distance in front of a seat reference point (SRP), (b) vertical distance above and below SRP, (c) lateral distance from the midline, (d) direction of thrust, (e) use of the steering wheel for 'bracing'. Equal numbers of male and female subjects were tested.

Miller (1983) set up a study to observe the actions of pickers and discovered that about 15,000 movements of the right thumb were made by a worker filling 30 nets - a day's work. Back pain is also a problem for sprout pickers because of the bent

position they tend to adopt while working. Dr. Miller has also treated several cases of frost bite of the fingers. Again he set up a study to examine the physiological effects of working in the cold and exposed conditions in which sprout pickers operate. On the day of the test the temperature was -2 deg C. Pickers start work at about 8.30 a.m. and their attitude to frost bite is that they do not worry when the cold causes pain - it is when they cannot feel their fingers that they are concerned.

Kaminaka et al (1981) studied the effects of steering only vs. steering plus rear monitoring on the operators' peripheral field of view, and the steering input frequency on operator performance. Response times to visual stimuli located in the visual sphere surrounding the operator were determined. Visual field contours derived from the experimental data were plotted and used to illustrate variations in the operators' field of view due to changes in the experimental variables. The operators of agricultural machinery are required to perform many tasks which require visual attention, both constant and intermittent. Similarly, the subjects in this simulated agricultural operation were required to perform three tasks which demanded visual attention:

(1) A steering task of varying frequency (analogous to varying vehicle speed)

(2) A rear monitoring task in which considerable amounts of eye, head, and body movements were required

(3) Subsidiary monitoring of light stimuli dispersed about the visual sphere surrounding the operator

Under the test conditions studied, the effect of the type of task on steering error rates was significant and dramatic. The sharing of attention between the two spatially disparate stimuli during the steering plus rear monitoring task resulted in large decrements in operator steering performance. Decrements in steering performance caused by increases in steering input frequency were even greater than those caused by differences in the type of task. The size of the operator's peripheral field of view had no statistically significant influence upon his steering performance. In the actual field operation of agricultural machinery, these results imply that heavier

workloads, whether imposed by additional visual monitoring or by higher vehicle speed, will result in poorer operator performance.

Maeda et al (1980) studied localized fatigue complaints and parts of the body where fatigue was felt during fruit picking among 49 female farmers engaged in greenhouse strawberry culture and 53 female farmers engaged in greenhouse eggplant culture. Furthermore, the bowing posture for strawberry picking was compared with that of eggplant picking using newly devised posture-pattern recording equipment. More than 50% of strawberry or eggplant farmers complained of fatigue in the lower back and shoulders. The prevalence of low back pain was significantly higher among strawberry farmers than among eggplant farmers, probably due to the deep bowing posture of the former during picking work. The new posture-pattern recording equipment proved useful for investigating changes of work postures.

Seppalainen and Uusitupa (1977) reported strawberry pickers' peroneal palsy. The common peroneal nerve is the most susceptible of the leg nerves to external or internal injury. Posture necessitated by occupation may lead to this injury as was noted as early as the 19th century. The most common occupations causing this occurrence are weeding beets, digging beets or potatoes or taking up peat and sometimes squatting. The symptoms commonly occur even after only a few days of work. Occupational injury to the common peroneal nerve seems to be relatively uncommon as judged from reported cases in the literature, as well as from inquiries to insurance companies dealing with occupational diseases and injuries in Finland. However, peroneal nerve lesions occur, and they may occur in clusters as we noted when 10 cases of peroneal paresis emerged among strawberry pickers during a few weeks within a small region of strawberry cultivation.

Weston and Espir (1977) presented two young patients with foot drop. Both had noticed weakness and tingling in the feet following a prolonged period of strawberry picking five days previously. These two young people had thus developed lateral

popliteal nerve palsies while picking strawberries. This appears to have resulted from local pressure on the nerve while squatting for several hours with the knee flexed and the outer part of the leg pressed on the ground with the foot extended and inverted. The girl was evidently in the same position with pressure on the affected leg for two to three hours, and recovery of her complete palsy is likely to be slow and possibly incomplete. With the man the pressure was maintained first on one side and then on the other and, as the palsies were incomplete, recovery may be more rapid in this case.

Jamieson (1969) discussed orthopaedic problems arising from farm work. The patterns of farm injury constantly change, and since mechanisation has become so widespread the pattern has tended to become less specific, for many farm injuries are now similar to industrial injuries.

Matthews (1967) examined the ergonomics aspects of transplanters. He suggests that two of the chief factors in the human aspects of their design are the posture of the operator and the nature of the working form of planting wheel and grip mechanism.

Laboratory examination (E.M.G.) of the operator posture on one transplanter revealed that a significant improvement is possible by alteration of the seat and footrest positions. Field trials confirmed the improvement in comfort of the modified machine and in a trial with relatively inexperienced operators (general farm workers) a significant improvement in worker efficiency was obtained. This was not shown to the same extent with very experienced farm operators. One possible reason for this may be that these operators, who were used to working on transplanting machines which required an apparently poor posture, may have become conditioned to the cramped position.

Future designs should incorporate a larger planting wheel than those generally employed on currently available machines, to allow a higher position for the plant transfer task with minimal bending of the body and to provide easy access.

Further work is necessary to establish the relative merits

of plant grips which may be individually closed (partially paced task) and the grips closing at a fixed point on the wheel's revolution (strictly paced task). The former appear likely to allow higher working rates and/or fewer errors but are likely to be more expensive to manufacture. The investigations already completed demonstrate the potential improvements in the human aspects of the design of transplanters, and similarly of other field machinery of this type (e.g. potato planters or harvesters).

Matthews (1964) reviewed research into factors affecting the ride comfort of tractor operators against a background of the existing knowledge of the effects of low-frequency ride vibration on man. This knowledge includes the influence of vibration on comfort, working efficiency and health. Comprehensive tests of tractor seat designs allow the mechanical requirements of an optimum seat to be formulated. The effect of seat position was also discussed. Suspensions for the tractor body or for an operator's cabin offer possible advantages. Other research investigations are proposed and the implications of formal measurements of ride comfort outlined.

# CHAPTER FIFTEEN

## STRESS AND FARM WORK

Gisele Ireland (1983) reported on a study by concerned farm women:

The definition of stress is as varied as the reasons that cause it. It is a feeling, a state of mind. It tells you that something is out of kilter, but at the same time, it can be a difficult condition to diagnose. The results of the survey were presented to many groups of farm women, and the women stated that it was easier to recognize stress in others than it was to define their own.

As spring planting progresses into the fall harvest, weather and time place stress upon the farmer. At this time the farmer and his wife operate at maximuin efficiency levels to ensure that the crop gets harvested. Stress makes them perform with enthusiasm and forces them to meet a set goal. Some control over their environment, and a degree of control over the outcome of their performance makes this kind of stress tolerable.

The women in the survey cited the factors that contributed to their stress on the farm. The main cause, lack of profit, was followed closely by other financial concerns. These were financial difficulties, lack of leisure time and lack of money for a holiday. Stress was evident when the cost of producing a commodity exceeded the return for their product by ever increasing margins.

Higher degrees of stress were cited in cases where financial problems were extreme. Once interest could no longer be paid on a bank loan, or the woman believed that the family would lose all or part of the farm that year, higher stress levels were noted. Other stress contributors were family responsibilities, expensive machinery repairs and other farm expenditures.

Record keeping and accounting on the farm fell mainly to the women, who were responsible for financial decisions concerning personal wants and needs and paying outstanding accounts. When financial situations deteriorated, there was the added stress of denying family members items that would normally be granted.

Mental fatigue was listed as the most common symptom of

stress. According to the women who discussed the survey information, mental fatigue was defined as an emotional state of indifference. The loss of an animal was greeted with the same degree of equanimity as the plugging of the sink. The woman no longer cared.

Frustration followed closely on the stress scale of symptoms. The women who were frustrated realized that no matter how much they put into the farm in hours or effort, it would make little difference in the end result.

The third most common symptom was irritability. Women found that minor things irritated them more than they would normally. Women also said that their performance was affected by this state of irritability and it seriously affected their relationships with family members and friends.

Sleeplessness was another stress symptom that was frequently reported. Some of the women who did sleep, wished they hadn't, since their rest was disrupted by nightmares.

The greatest degree of stress was reported by the younger women (25 to 34), especially if they had just started farming and were raising a family. All stress levels were at the highest point in cases where they could no longer pay the interest on their loans.

Ireland (1981) in a brief presented to the Ontario Federation of Agriculture Task Force on the Financial Crisis speaks of the psychological effects of financial stress on farm families. Farm wives are not solely concerned with what is happening financially, they are deeply concerned with the psychological effects facing their families and communities today. Financial stress colours their thinking and actions to produce apathy, frustration and hostility. They are using facts which were obtained collectively from about one hundred situations that have been dealt with in the Grey-Bruce area.

The farmer has accepted a lower rung on the social and financial ladder for so long that he has been conditioned to think he is lucky if he breaks even. The farmers are now hostile and don't care who will go hungry if they stop producing, as long as he isn't losing doing it anymore.

Farming is a life time commitment. Financing the farmer should be the same. Short term financing with a floating rate of interest has been suicide for farmers. Interest rates should relate to the price of the product in question. If government is so dedicated to a cheap food policy...it should be prepared to offer cheap interest to produce cheap food. Farmers would operate more efficiently if made aware of what products to produce and what is a glut on the market. Allowing farmers to phase out of unprofitable commodities would certainly be preferable to bankruptcy. Farmers should have plans devised that look years ahead for demand and consumption patterns so that they can tailor their operations to meet the demand.

A report on the Women of Unifarm Spring Program 1979 deals with coping with stress on the farm. A series of workshops dealing with coping with stress on the farm were held throughout the Province of Alberta in April of 1979. The workshops were jointly sponsored by Women of Unifarm, Alberta Agriculture and the Department of Labor (Farm Safety Program). The women attending the workshops identified and priorized the stresses that they felt affected them. The categories were:

| | |
|---|---|
| Finance | Weather |
| Family | Community Social Problems |
| Work | Retirement |
| Land Use Issues | Time |
| Farm Management | Environment |
| Health | |

They also identified the various agencies and services outside the home that could help ease the stress.

Crocker (1978) commented on stress and the farm family. Stress is becoming increasingly important to corporations and to individuals in almost every walk of life. Farmers are no exception.

Niskanen et al (1975) carried out a study of attempted suicides in urban versus rural areas, with a follow-up. The group of subjects consisted of 44 patients (attempters) who were admitted to hospital for treatment because of attempted suicide during a 3-month period in Northern Savo (in Eastern Finland),

another 44 patients (non-attempters) admitted to hospital in the same period for other reasons serving as controls. The number of women was the same in both groups, and so was, in consequence, the number of men. The study compared the attempters with the non-attempters and, in addition, the patients coming from urban areas with those coming from rural areas, the ratio of the urban to the rural patients being the same in both groups. The study was based on personal psychiatric interviews with the patients, which took place in each case both immediately following the patient's admission and precisely 3 months afterwards. The results showed that schizophrenia was significantly more frequent in the rural than in the urban attempter group. By contrast, alcoholism and alcohol abuse were more frequent in the urban than in the rural attempter group. Compared with the urban patients, the rural patients tended to be psychically more seriously disordered. Poisoning by drugs was a significantly more frequent means of attempted suicide in the urban than in the rural group. The patients in the latter group, again, had resorted oftener to the so-called "active" methods of attempted suicide. Of the attempters, 25% attempted suicide anew during the 3-month period, the corresponding figure, for the non-attempter group being only 6%. During the follow-up period, a greater number of suicidal attempts was made by the patients in the rural group than by those in the urban group, and, as regards the intent to succeed, the attempts of the former were more serious than those of the latter. The so-called "active" methods were used more often by rural than by urban patients also during the follow-up period. All in all, the self-destructive behaviour exhibited during the follow-up period was graver in the rural than in the urban group.

Brown and Prudo (1981) reported that an earlier survey of a random sample of women in Camberwell in South London has shown that the majority of new occurrences of depressive disorders were brought about by certain kinds of life event and ongoing difficulty (provoking agent) and that the risk was increased under these circumstances by the presence of certain other social factors (vulnerability factors). Working-class women were much more likely to develop depression because they experienced more of these factors. A new survey in a rural population in the

Outer Hebrides has confirmed the importance of these factors in the genesis of depression, although provoking agents occurred much less frequently in this rural setting. However, integration into the traditional way of life, rather than a middle-class status, was related to a lower chance of developing depression, and this appears to be explained by the relationship of provoking agents and vulnerability factors to such integration in the Outer Hebrides, and to social class status in Camberwell.

Valkonen (1982) describes differences in mortality from ischaemic heart disease (IHD) and other selected causes of death according to region, marital status, language group (Finnish vs Swedish), social group and rural-urban divisions in Finland. The data include all deaths in Finland during 1971 - 75 in the cohorts of men aged 35 - 64 and women aged 35 - 74 on January 1st 1971 (33,862 IHD deaths). The sociodemographic characteristics of the deceased were obtained through computerized linkage from the records of the 1970 census by means of personal identification codes. IHD mortality was found to be higher than average in Eastern Finland, in the Finnish speaking population and in lower social groups. There was a higher mortality in non-married than in married categories among men, but among women the differences were smaller. The findings are discussed in the light of differences in stressrelated mortality.

S. Pfeiffer et al (1984) did a survey of the aspects of physical fitness and health in Ontario dairy farmers. The ultimate objective was to determine whether farmers enjoy certain health advantages over their urban peers. A sample of 106 male dairy farmers, aged 32-67 years, from Wellington County, Ontario, were examined for a range of anthropometric, physiological and psychosensory variables. Results indicate that this sample differs from contemporary urban males within some age groups in ways which are likely to indicate the chronic effects of the farming lifestyle. These deviations include lower estimated percent body fat, very high grip strength values, reduced back flexibility, possible industrially-related hearing loss, certain low pulmonary function values, high energy intake and low HDL:

total cholesterol ratio.

Stress among persons engaged in farm work is of major concern. Methodological challenges should not discourage future research in this area as it pertains to Ontario.

# CHAPTER SIXTEEN

# SUMMARY AND FUTURE DIRECTIONS

## Introduction

In this document, the scientific literature pertaining to the health of persons engaged in farm work has been reviewed and organized in such a way that would be useful for the Occupational Health and Safety professionals interested in this matter. The objective of this chapter is to summarize and highlight important issues from this comprehensive review. The information presented in this chapter is aimed for the general public and policy planners who are considering priorities for further action that pertain to Ontario.

## Approaches to Prevention

Prevention is in an exciting state of flux. It has long been recognised that physical, chemical and biological factors in the environment affect health. From a health perspective, it is now increasingly the case that the environment is seen as including economic and social factors. There is a growing awareness that these can have harmful as well as beneficial effects and that selective economic and social development is needed to maximise health benefits.

Prevention can partly be understood as paying attention to the physical, chemical, biological, social and economic environments with the aim of reducing accidents, illness and death. Prevention is also concerned with health education and preventive services such as screening. It is customary to describe the many and important aspects of prevention that are concerned with the work environment as being within the province of occupational health.

Prevention can also be distinguished from health promotion. The latter includes prevention but also embraces ideas of

positive health. The usefulness of this term can best be demonstrated in the field of mental health. It is clear that some psychiatric disorders can be prevented but, having said that, there is also a difference between individuals who are "coping" and individuals who are "thriving". In this field , prevention only seeks to ensure that people are coping, that they are free from psychiatric illness. Health promotion also aims to produce thriving, fulfilled people. It is interesting to note that health promotion seems much more in tune with the World Health Organisation's definition of health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".

A widely used classification divides prevention into three types according to the purpose of the activity. Primary prevention seeks to prevent diseases or accidents from ever occurring. Secondary prevention tries to detect disease in the earliest stages and while it is still treatable. Screening falls into this category. Tertiary prevention attempts to prevent deterioration in established disease. Attempts at health promotion introduce the added goal of well-being.

The scope or range of preventive measures can be illustrated by reference to another widely used classification, this time concerning the variables in the dynamic processes which determine our health - agent, host and environment.

An agent is taken as any specific substance or environmental condition that acts on people to produce disease. Biological agents, such as bacteria are responsible for infectious diseases while organic and inorganic substances produce acute and chronic conditions. Agents can be identified both within and outside the human body and may act singly or in combination. There is therefore very wide scope for actions that can be taken to achieve primary prevention. They range from the control of airborne chemicals or dust in industrial processes to regulations governing the preparation of food.

Agents obviously vary in their potency just as hosts vary in their susceptibility - the environment affects them both and the relationship between them. Prevention through action on the environment can moderate the biological environment; the chemical environment; the physical environment; the social environment and the economic environment.

Actions directed at the hosts are generally concerned with immunity to the effects of particular agents, with health education and with other preventive services. Immunity is partly developed naturally and partly acquired through immunisation. Of importance in determining the spread of epidemics is the proportion of the population with immunity. If this is sufficiently high then epidemics can be slowed down or stopped in rather the same way as firebreaks act to control forest fires. Such simple opportunities to prevent illness from chemical hazards do not exist and emphasis on the latter two approaches must be considered. The scope for action on hosts is increased when health education and preventive services such as screening are implemented.

When considering the range and type of prevention necessary in Ontario, whether in the form of services or other actions, it is clear that it should be related to the burden of accidents, illness and mortality actually present in Ontario. There is a clear trend in patterns of mortality related to economic and social change. In industrialised countries, for example, at the end of the 19th century and in the 20th there was a decline in the toll of infectious diseases and an associated increase in chronic and degenerative conditions.

Three important points can be drawn from studies of this process. First, the major falls in mortality came before the advent of modern methods of medical treatment. The improvements in health were largely a result of better nutrition, cleaner water supplies and safer waste disposal. Modern scientific medicine played a relatively minor role. The argument that health is not the result of simply providing health services is also supported by experiments in developing countries. The

evidence suggests that a much broader, prevention-orientated approach is required.

Second, the evidence from industrialised countries shows that treatment services are often ineffective and typically inappropriate when considering the chronic diseases and how best to deal with them. Contrary to the all-conquering image of modern scientific medicine, it makes no sense (either financially or in terms of human suffering) to see late and dramatic surgery or prolonged chemotherapy as the answers to the problem of heart disease or lung cancer. While treatment certainly provides some benefits, much more attention has to be paid to prevention before it will be possible to break the pattern of damage over a lifetime being followed by late and often ineffective repairs.

Third, it seems that the etiology of the chronic diseases and conditions is inextricably bound up with the very processes of development which were associated with the decline of infectious diseases. Under-nutrition, for example, is linked to host vulnerability to a wide range of infectious diseases while over-nutrition has been associated with increasing coronary heart diseases. Many other chronic diseases and the type of accidents characteristic of industrialised societies are bound up with social and economic conditions and are consequently very difficult to remedy. While preventive measures such as immunisation are relatively easy, attempts to modify the social and economic environment impinge on many more people and groups and meet with more resistance.

Scope of Potential Health Problems

Farm work in Ontario is a key industry and an examination of potential risks that confront the farmer, farmer's family and farm workers has been commissioned as a first step to examining the potential courses of action to protect and prevent occupational diseases and accidents to persons engaged in farm work in Ontario. In spite of the many shortcomings of the quality of evidence relating farm work and health, the scientific

literature contains at present important information of both descriptive and analytical types that is useful to apply to the study of the health of persons engaged in farm work in Ontario.

Machinery and chemicals are used throughout the agricultural cycle. Tractors, spray rigs, moveable tins, conveyor belts, hauling trucks, ladders, hoes, axes and saws are all used routinely by farmers. These dangers are clearly visible however, the health risks posed by agricultural chemicals may be more ubiquitous. The reason for this is that these problems are chronic diseases that take often many years to develop from the time of initial exposure to the recognition of an adverse health effect. The time period between the exposure and the presentation of disease is called the latency period and often with respect to cancer, this may take a period of 15 to 20 years to develop. The recognition of reproductive disorders are in contrast much more immediate but the linking of a particular occupational exposure such as a pesticide and the adverse reproductive event such as a spontaneous abortion, birth defect, or behavioral problem in an offspring may be more difficult to relate due to the complex nature of the stages of human development. Neurological disorders are often very subtle and hard to recognize early in their course of development. By the time a major disease of the brain is diagnosed by current medical technology, the condition is usually irreversible and resistant to current modes of medical therapy.

The application of the large body of scientific literature specifically to agricultural conditions in Ontario is a much more difficult task for several reasons. There is a general lack of information available regarding exposure to pesticides and organic chemicals in Ontario. There is also a lack of awareness on the part of the agricultural community and the medical community as to the dangers involved with exposure to these toxic substances. The information collection system for agricultural health and safety in Ontario is clearly inadequate. For example, basic hospital medical records and government morbidity and mortality statistics do not have necessary information of sufficient reliability and validity to assess the relationship

between occupational diseases and specific chemical exposures. The occupation of a person with a specific disease that may cause an admission to hospital or utlimately result in death, is currently not recorded and if any relationship is to be drawn, complex record linkage with computer databases are required. This is very time consuming and expensive. Other approaches to actually search and trace the occupation of the individual stricken with a disease are very time consuming and tedious and may not necessarily result in valid relationships being drawn.

Another possible reason for the general lack of information concerning the health of persons engaged in farm work in Ontario stems from the difficulty in carrying out scientific field studies of agricultural workers. It is well known that there are more agricultural farm workers in the world than any other occupational group. In many respects this group of workers has the broadest and most extensive of occupational exposures to biological, chemical, and physical agents of disease or injury. Even though in this document a comprehensive review of all available scientific information has been carried out, the full spectrum of all health hazards to these workers remains obscure with respect to a well-defined population at risk. The nature of the agriculture community makes this difficult as often there are many migrant workers involved in seasonable types of work activities. This makes following persons exposed to a particular hazardous substance over many years of time very difficult and therefore the end result in terms of burden of disease often cannot be established with certainty. Also the nature of farm work is such that a given individual farmer may be exposed to many different types of hazards and may make the association between specific occupational exposures and the disease difficult.

The challenges confronting the scientists designing field studies of farm workers include the wide variety of diseases related to the work task involved, the highly changeable work environment, frequency and mobility of workers and work, the absence of high quality medical care and record keeping, the lack

of data related to the nature and degree of occupational exposures, and the absence of measurable indices for subtle monitoring of health effects from farm work.

In spite of these methodological challenges, a number of key studies have been carried out in the world. A study done in Southwestern Ontario by Sullivan et al during the summer of 1979 attempted to address the problems encountered during the course of their work. Their conclusions were that the health consequences of the many hazards were probably much underestimated. Much of their analysis focused on farm accidents; however, they did express concern about the effects of toxic chemicals.

Other studies concerning the general health of farm workers include those by Gallagher (1984), Stubbs (1984), Burmeister and Morgan (1982), Carlson and Peterson (1978), Bleiweis (1977), Husman (1982), Thelin (1980), and Dubrisay and Pages (1978) which all point to the unusually high rate of mortality among farmers from the various types of diseases and accidents. Husman in his study concluded that occupational health services to farmers should be aimed at the prevention of accidents and diseases of the skin, respiratory and musculo-skeletal system. Navakatikian (1980) noted that among machine operators, the rates of chronic bronchitis, digestive disturbance and hearing loss seem to have now decreased due to design of machinery, while cardiovascular and nervous disorders have shown an increasing trend due to intensification of work. Studies conducted by Suskind and Hertzberg (1984), Morgan (1980) and Wang and MacMahon (1979), show unusually frequent skin problems among workers exposed to different pesticides. Other researchers such as Lang (1982) and Ditraglia (1981) showed workers exposed to various pesticides have significantly higher rates of lung fibrosis, pneumonia, and respiratory disease.

Health problems among farm workers exposed to agricultural chemicals are varied and affect many different systems. Acute health problems such as neurological disorders caused by these chemical exposures are easier to document than chronic diseases. Farm workers are exposed to a wide range of chemicals in their

workplace and therefore it is often very difficult to point out one chemical as the cause of the problem, particularly in terms of the development of chronic illnesses. One example of this is a study by Bogden (1975) which attempted to delineate the deleterious effect which pesticide exposure may have on migrant farm workers. They concluded that four major categories of pesticides: 1) heavy metal-containing substances, 2) chlorinated hydrocarbons, 3) carbamates, and 4) organophosphates present a major hazard and perhaps the most serious with regard to migrant farm workers, was organophosphates. In Ontario with offshore workers from the Caribbean and Mexico, migrant workers from Quebec and Northern Ontario, and the large resident immigrant population, a similar situation exists. Many of these workers are unaware of the dangers and the symptoms of pesticide poisoning. Should a possible problem arise, these workers are currently without protective legislation.

Causal Inference From Epidemiological Studies

Epidemiology is the study of the distribution and determinants of diseases in human populations. It includes two bodies of knowledge: epidemiological methods of investigation and epidemiological contents generated by the application of such methods. Epidemiological contents are notions on the health profile of communities such as those persons engaged in farm work and on the distribution and causes of specific diseases. These can be analyzed at a population level so that environmental factors as well as medical, technological, and social interventions particularly of a preventive nature can be evaluated.

It must be stressed that clinical medicine which traditionally includes diagnosis and treatment of a specific disease must include epidemiological information such as what is contained in this document. Epidemiological studies that describe and analyze the distributions and determinants of disease can be very helpful in reaching an in-depth understanding of the causes of a particular work-related health problem as well as pointing to

specific ways to prevent the problem. In this sense epidemiology can contribute in three main ways:

a) identification of environmental hazards related to work;

b) monitoring of the health effects of changes in the working environment including the enforcement of primary prevention methods. This may include engineering controls and the effect of legislative limits on toxic exposures;

c) evaluation of the usefulness of secondary prevention measures, for example biological screening and testing of exposed populations.

There are two main types of studies which are generally used. Those of the descriptive type analyze the patterns of the distribution of a disease or symptoms in a particular population of interest. The more sophisticated type of design is an analytical study which is able to test hypotheses about causal or etiological factors in humans. The specific study designs have been described in detail noting their important strengths and weaknesses in Chapter Three.

The problems of epidemiologic studies and their interpretation lie in the ability of the reader to critically evaluate the studies and be aware of major methodological flaws. Bias is a systematic error introduced by the investigator with or without intent. This is introduced by some factor in the study design which can be in any direction and is often not predictable. Random error, however, is not bias as it applies equally to both groups, that is exposed and non-exposed. By eliminating as many sources of bias as possible, the objectivity of the data that is collected and analyzed is maximized.

The main problems of epidemiological studies often originate with an unclear statement of the study question. Often studies have arisen out of political furor and this sometimes results in an unclear statement of research objectives. Secondly, the availability of data is often limited such that reliable and valid information cannot be incorporated into the study. For example, workers exposed to a potentially toxic substance often

find difficulty in knowing its true chemical constituents as many chemical manufacturers are protected by trade secret laws. Also the routine collection of health information in a particular group such as farm workers are not kept in a comprehensive or systematic fashion. This leads to a major measurement problem when trying to link exposures from farm work to the health status of farm workers. Even when information has been collected the analysis and interpretation of any studies are limited.

The shortcomings in the quality of evidence that exists on this topic must be recognized by the consumers of this information and be cautious in the interpretation of studies that have methodological defects. It is therefore of great importance that studies that are to be carried out in the future be optimally designed to minimize any possible methodological errors. Specific criteria for the design and interpretation of these studies have been outlined and these should be adhered to as much as possible.

The next section identifies major priority health problems among persons engaged in farm work. The summaries on each specific condition are related back to the in-depth literature reviews done in previous chapters. The nature of the scientific information is discussed from an interpretive point of view.

## Ten Priority Health Problems Among Persons Engaged in Farm Work

### Problem 1 - Cancer

There is mounting evidence in the scientific literature that modern farming practices may lead to a significantly greater risk of dying from certain kinds of cancer.

Reviews carried out by Health and Welfare Canada (1982) and Blair (1982) point to specific cancers such as leukemia, (a cancer of the blood), lymphoma (a cancer attacking the lymphatic system) and multiple myeloma (a cancer that attacks the bone and bone marrow). These reviews suggest that the risk of developing these types of cancers are elevated in certain types of farming,

for example across poultry, dairy, grain, livestock as well as general farming.

The specific cause of these types of cancer has yet to be identified from the many studies reviewed. Many of the studies published have been done in the mid-western United States. For this reason, for example, leukemia has been implicated in corn production and more specifically, the fertilizer type used may in fact be the true causal agent. Burmeister (1982) found this relationship linked to corn produced per acre as well as the number of milk cows and the number of egg-laying chickens. The study by Blair and Thomas (1979) also suggested a relationship to heavy corn-producing counties. Blair and White (1981) found also that there were elevated risks to the development of leukemia in those counties with heavy dairy production and fertilizer use. Other suggestions from the studies by Milham (1971) and Priester (1970) relate dairy farming to leukemia as well as other types of blood cancer. Many other studies have related lymphoma and Hodgkin's disease to farming. These studies however are not as detailed and do not distinguish between types of farming or any suspicious exposures. There is more suggestive evidence relating multiple myeloma but again no specific agent or type of farming has been implicated.

Cancer of the respiratory tract including nasal cancer, laryngeal cancer (throat cancer) and lung cancer suggest a relationship to different types of farm chemicals. For example, Hardell (1982) suggested that chlorphenols present in wood dust are related to nasal cancer, however, Hernberg (1983) did not find any relationship. With regards to lung cancer Blair (1983) found an elevated rate among pesticide applicators and Rothschild and Mulvey (1982) found an elevated risk among sugar cane farm workers. There is suggestive evidence that pesticides, particularly of the organophosphorous and organochlorine types, are the putative agents as has been suggested in many animal studies. The confounding factor of cigarette smoking, however, was not well-controlled for.

Soft tissue sarcoma, a rare type of connective tissue cancer, has been a topic of much research due to a suggested link

with a chemical called 2,4,5-T, a phenoxy acid. Balarajan and Acheson (1984), Hardell and Sandstrom (1979) and Eriksson (1981) have done studies that demonstrate some type of relationship. There are other studies such as Zack and Suskind (1980), Cook (1980) and Ott (1980) which did not find a relationship, however, those studies were done in manufacturing situations. Animal evidence gives these possible associations some biological plausibility.

A large number of studies have demonstrated an increased risk of stomach cancer with farming. These studies done again in Iowa by Burmeister (1983, 1981) and Bueschling and Wollstad (1984) and Armijo (1975) have pointed to a problem. There is only a slight suggestion that this may be related to dairy farming and/or nitrate fertilizer usage. This relates back to some evidence that N-nitroso compounds induced tumors in animals. There are a few other human studies that relate to liver cancer, pancreatic cancer and colorectal cancer in farming.

Cancer of the male reproductive system such as testicular cancer and prostatic cancer has been explored by a number of studies which demonstrate conflicting evidence for and against an association with farming. Further studies clearly need to be done. Bladder cancer elevated risk has been demonstrated in two older studies, one by Milham (1974) and Decoufle (1973) in wheat and cattle farmers, however this has not been confirmed among dairy farmers in a study by Blair and Watts (1980).

Elevated risks of brain cancer have been demonstrated in a number of different types of groups including those exposed to insecticides and as well dairy and cattle farmers. The studies were more descriptive in nature and point to a potential problem and further research must be done. Skin cancer has been linked in agricultural workers by studies by Lindqvist (1981), Wiklund (1981) and Whitaker. The main exposure of concern is that to ultra-violet radiation from the sun.

The possibility of a cancer problem among Ontario farm

workers remains to be explored. This area is a very high priority and needs to be acted upon as soon as possible. One of the recommendations of this report is to set up a comprehensive health surveillance system that will monitor cancers in Ontario and link them to occupational exposures including that of farm work. A large scale case-control study could be organized if this type of surveillance system was in place. Linkages with centres of expertise in epidemiologic research could carry this analysis further to explore not only the type of farming but specific exposures encountered such as that to agricultural chemicals.

Until these relationships are recognized, comprehensive preventive approaches to reducing the risk of the development of cancer among farm workers will be obscured due to lack of data. Inferences and projections from laboratory toxicological data in animal studies are useful adjuncts to human toxicological information and have been helpful to pointing out the potential problem situation. The epidemiological studies that have been reviewed identify the existence of a problem that may confront persons engaged in farm work in Ontario. These and other studies have been summarized in tables reviewed in Chapter Four of this document. They are extensively examined with respect to the quality of evidence with regard to causation.

Problem 2 - Reproductive Hazards

The effect of farm work on reproduction may disrupt both male and female processes as well as poison the developing embryo and fetus. Human reproduction is very complex and exposures such as that of agricultural chemicals may disrupt these delicate processes at any point. Shepard (1983) has listed hundreds of chemicals that may affect the reproduction of animals, however, few of them have been confirmed to adversely affect human reproduction. The type of reproductive problems that can be expected are disrupted sperm production in the male and menstrual irregularities in the female. Problems such as spontaneous abortions, premature infants, stillbirths and neonatal death, and most importantly congenital malformations can

all be related to occupational exposures.

Whorton (1977 and 1979) has observed that a chemical DBCP has disrupted sperm production dramatically in exposed male workers. Levine (1983) confirmed this relationship. Insecticides such as carbaryl have been found by Wyrobek (1981) to have a similar affect on sperm.

Spontaneous abortion has been a topic of much study in Finland especially by Hemminki (1980 and 1981). Finland has a sophisticated adverse reproductive event surveillance system such that any possible relationship to occupation can be explored comprehensively. From his data there is some suggestion that agricultural chemicals are related to spontaneous abortions.

Congenital malformations have been the most important reproductive problem that has undergone study. The report of the New Brunswick Task Force on Chemicals in the Environment by Hatcher and White (1985) has related agricultural chemical exsposure to elevated rates of adverse reproductive outcomes in the Saint John River Basin area. Initially it was suggested that chemicals from the forestry spraying were the causal factors, however, their study demonstrates a clearer relationship to that of exposure to agricultural chemicals. Williams (1981) investigated the risks of congenital anomalies in the Holland Marsh area in Ontario, however, the study was not conclusive. Further more sophisticated studies such as the New Brunswick investigation are required to further explore a possible relationship. Other studies from around the world include that of the mid-western United States, New Zealand, Australia, and England and Wales. These implicate agricultural chemicals as being associated with types of congenital malformations involving the neural tube of the developing human.

It must not be forgotten that exposures to the mother in the post-natal period after birth may also adversely affect an infant. A number of examples such as that of 2,4-D, methoxychlor and various insecticides including organophosphates and

carbamates have been shown to be transmitted through the breast milk to the baby. These have resulted in a number of problems such as endocrine abnormalities as well as the possible risk of cancer later in childhood.

The evidence from the scientific literature indicates that exposures encountered in both males and females from farm work can disrupt human reproduction at a number of critical points. Not only does this problem in Ontario need to be researched more carefully, but farm workers must be made aware of the potential hazards so that preventive strategies can be initiated. Personal tragedies are inevitably involved when defects are present at birth or appear in later life. The need for detection of toxic agents to the embryo and fetus, the assessment of health risks, and the prevention of unfavourable outcomes of pregnancy need to be given much higher priority. Differences between animals and humans in metabolism, inherent sensitivity, and levels of exposure may be responsible for the differences observed between animal studies and humans observations. Among the problems in conducting epidemiological studies is the detection of chemically induced anomalies agains a background of sporadic defects. The size of scientific studies necessary to detect changes in the rates of some rare abnormalities is so great that such studies may not be feasible. Smaller studies may have problems which result in innacurate risk estimates.

An improved centralized system of registering birth defects and the input of occupation onto hospital admission forms would assist in the monitoring and prevention of congenital malformations induced by parental occupational exposure to hazardous substances. Although it is difficult to pinpoint teratogenic agents based on changes in the rates of a particular defect or constellation of defects, monitoring systems can provide clues to hypothesis testing in epidemiological investigations. Monitoring systems have been established on an international basis and are beginning to be established in Canada. Unless these efforts are supported they will always suffer from incomplete and possibly unreliable information. It is important to note that in Ontario, an extensive and complete

surveillance system exists for infectious diseases. The Ontario Ministry of Health monitors notifiable diseases such as influenza and sexually transmitted diseases. Trends are reported frequently to all health professionals concerned with the recognition and prevention of these infectious diseases. It is well within the capability of existing structures in Ontario to provide a similar type of surveillance for adverse reproductive events.

Problem 3 - Neurological Diseases

Diseases of the nervous system including the brain, spinal cord, peripheral nerves and muscles have been well understood and investigated for many years. Pesticides used in farming have been implicated in the cause of these diseases both acutely and in chronic forms.

Agriculture makes use of large quantities of various organophosphorous pesticides. Although these pesticides differ much from each other with regard to the degree of toxicity, and to physical, chemical, and biological properties, they have a number of effects in common which affect primarily the nervous system. These compounds are used widely in agriculture to control insect pests, acarids, nematodes, plant diseases, weeds. They are extensively used on fruit trees such as apple, pear, plum and citrus trees, vegetable crops, ornamental plants, cotton and cereal crops. These pesticides are rapidly absorbed through the mucus membranes of the digestive tract, respiratory system and skin and are conveyed by the blood to various body tissues.

Certain compounds are active cholinesterase inhibitors and others are transformed into such inhibitors after absorption in tissues. This process is carried out by the liver and can interact with other chemicals or drugs. The mechanism of toxic action is an inhibition of the esterase enzyme activity, in particular cholinesterase, which plays an important physiological role. This affects both the central and autonomic nervous systems where acetylcholine acts as a mediator nerve impulses.

The initial symptoms in their most severe presentation may include convulsions and paralysis. The first stage of poisoning is characterized by anxiety, nausea, salivation, vomiting, abdominal pains, diarrhea, blurred vision and excessive tearing. The early symptoms of poisoning such as dizziness, nervousness, anxiety and agitation may be present before or after the nausea occurs. Symptoms of moderate poisoning are headache, impairment of sensitivity or feeling, sleeplessness or on the contrary sleepiness, confusion, ataxia or staggering, tremor of the hands and head, loss of orientation and speech disturbances. At later stages blood pressure may become unstable before death and pulmonary edema and collapse may occur. Loss of control of urine and feces occurs. Finally respiratory paralysis results in death. After an episode of acute poisoning, headache, dizziness, sleepiness, loss of appetite and general weakness may last for many weeks or even months. Problems such as trembling of the hands, nystagmus (a visual control problem), and psychic disorders may occur after an acute toxic event.

The diagnosis of organophosphorous poisoning is made by the measurement of a pronounced decrease of the blood cholinesterase activity in the blood. In mild cases the level may not be depressed significantly as often the blood test sample is not taken at the optimum time of acute poisoning. This diagnostic test usually indicates significant exposure if depressed and eventually returns to normal if exposure is stopped. Treatment is well understood with the use of atropine and pralidoxime.

The recognition of this condition is problematic. Many physicians have not been trained adequately in recognition of acute toxic exposures such as that of organophosphorous and/or carbamate compounds. The latter type of poisoning has a similar mechanism and clinical presentation, however, the treatment is different. The addition of pralidoxime must not be initiated for the management of acute syndrome. The manifestations of chronic poisoning are therefore often unrecognized as the subtle neurological problems may be confused with other types of

conditions.

The issue of delayed neurotoxicity is one of growing controversy. The clearest under standing of the mechanism of this phenomenom, which involves a delayed destruction of peripheral nerves after exposure to organophosphates, is described by Lotti (1984). A screening test called neurotoxic-esterase may be used to monitor for chronic effects, however, this is yet to be tested in field studies. This would be an area of high-priority research given the large extent of exposure to these types of compounds in Ontario.

Hirshberg and Lerman (1984) describe a computerized medical information system which is able to track and cross-tabulate data with regards to patients who were poisoned with organophosphate pesticides. This type of information database will be crucial to the further understanding of the acute and chronic problems from these types of incidents.

The basic approach to prevention of pesticides poisonings and therefore the reduction of neurological diseases lies in proper storage and preparation of pesticides, proper spraying techniques with minimization of exposure during spraying, and the implementation of spraying time and rules. Personal protective equipment may be used to minimize exposure through the respiratory tract to the skin, however, problems with comfort and heat often limit the feasibility of long-term wearing of these devices. Medical surveillance may be of use to monitor blood cholinesterase levels and in certain jurisdictions this is mandatory. Proper medical aid must be available through local emergency departments.

These preventive strategies are easily stated, however, the implementation of this in the field and within the health care system will be a major challenge for Ontario. Persons engaged in farm work are not educated as to the toxic affects of these types of substances and therefore the health problems are often unrecognized. Blood testing is not carried out on a systematic basis and this may be a priority area for legislative

intervention. Emergency departments are generally not equipped or prepared to deal with toxic emergencies of this sort. Through an extensive physician education program it has been proposed that the recognition and treatment of pesticide poisoning would be a high priority topic.

Further research must be carried out into the chronic effects of these neurotoxic substances as the scientific literature has only begun to reflect an understanding of this phenomenom.

Problem 4 - Skin Disorders

Any abnormality caused directly or indirectly by the work environment is an occupational skin disorder. Work-related skin reactions from farm work are as varied as the environments in which people work, although contact dermatitis may be by far the most common problem. The skin is the boundary between humans and their surroundings and it is therefore very often the first site exposed to environmental contact. Farm workers have a definite risk of developing work-related skin disease compared to other industries.

The human skin except for the palms and soles is quite thin; yet its variable thickness, its collagen and elastic components allow it to function as a flexible barrier. It is a unique shield which protects within limits against mechanical trauma, penetration by various chemical agents, water loss from within, microorganisms, natural and artificial light, and stress levels of heat and cold. The various layers including the outer layer of dead cells (keratin) are susceptible to organic or inorganic alkaline compounds. These compounds tend to soften but not dissolve the keratin cells preserving the intactness of this layer. Other types of substances such as solvents will also weaken the barrier effect and thus allow other chemical agents to enter the body. Ultraviolet radiation protection is provided by the pigment (melanin) manufactured by the melanocytes located in the basal cells of the epidermis. The heat exchanging effect is

essential to life. This includes sweat gland function, vascular dilatation and constriction, and nervous control. Disruption of these mechanisms result in heat and cold disturbances. More recently the immune function of the skin has been recognized and these disturbances may result in types of hypersensitivity rashes.

The causes of skin disorders among farm workers can be classified as mechanical, physical, biological and chemical. Predisposing factors may include race, skin type, other skin disease such as acne, eczemas and fungal diseases, and general lack of cleanliness.

The symptoms of skin disorders may be characterized by an acute contact eczematous or weepy dermatitis. These are clearly the most common type of rashes seen and they may develop into a chronic problem. These are often hard to treat and require cessation of exposure and creams of various pharmacological types. Other types of reactions include photosensitivity dermatitis, which can be problematic for a farm worker exposed to sunlight. Many types of chemicals such as creosote, pitch, and anthracene as well as drugs can cause a photoreactive response in the skin. Some types of plants of the family umbelliferae can cause a similar reaction. These plants include cow parsnip, celery, wild carrot, fennell and dill. Acneforme lesions and folliculitis can occur in workers exposed to heavy soilage. These occur anywhere on the body, especially on the forearms, thighs and buttocks. Acneforme rashes are related to a number of agricultural chemicals, especially those contaminated with dioxin. Chloracne is an important skin disease that should be investigated among Ontario farm workers.

Very common sweat-induced reactions (prickly heat) are found among farm workers. Pigmentation changes can occur induced by hydroquinone compounds which may be used during the course of farm work. Various ulcerations can be induced by compounds containing chemicals such as chromic acids, potassium dichromate and arsenic to name a few.

The most serious concern is that of malignant disease of the various layers of the skin. These may occur from the squamous cell layer, basal cell layer, and melanocytes. A high index of suspicion must be maintained with regard to any type of new growths on the skin and biopsies must be taken to clarify the diagnosis. By far the exposure to ultraviolet radiation is the main potentiating factor, however, certain agricultural chemicals may also have some role to play.

The diagnosis of occupational skin diseases are complex especially if chronic in nature. If an allergic type response is suspected or documented, the management of the job placement is difficult. Cessation of exposure will help the condition, however, upon reexposure the symptoms may reappear often with increasing response. Prevention by minimization of exposure to the skin is crucial. By meticuluous hygiene practice as well as the use of protective equipment to minimize cutaneous exposure, the problem of sensitization may be diminished. Patch testing of the skin may be useful either as a preplacement examination or as a diagnostic manoeuver to understand an immune response to an occupational or non-occupational exposure. Appropriate medical and referral of services must be provided to farm workers so that these very common and often serious disorders can be managed properly.

Problem 5 - Lung Diseases

Farm workers' lung diseases can be related to many types of exposures that occur during the course of farm work. Respiratory problems that present as shortness of breath can be related to three common causes: 1) Occupational asthma is usually recognized by the patient as being associated with specific activities. Commonly it starts shortly after he or she enters a particular area or is exposed to a certain substance. It also may be associated with a runny nose or tearing of the eyes, 2) Farmer's lung which is very common typically presents as an acute attack of fever, malaise and breathlessness four to six hours after handling mouldy stored hay, and 3) Silo filler's lung occurs

after exposure to oxides of nitrogen from the top of an unventilated silo. These types of diseases are well reviewed by Seaton (1984).

Farmer's lung will be common in dairy farmers who are exposed to a large amount of hay which may be mouldy. Exposure to organisms including the various types of fungii such as micropolyspora faeni, thermonospora virrdis, and thermoactinomyces candidus induce a general type of allergic disease. This problem often can be misdiagnosed by doctors as being a common cold, flu, bronchitis or pneumonia and it is not surprising that the prevalence of this condition is underestimated.

Wells (1980) did a review of farmer's lung for the Farm Safety Association of Ontario and concluded: 1) The possibility of farmer's lung should be considered in any farm worker suffering from breathlessness without evidence of cardiac failure or airways obstruction, 2) Farm workers who have an acute reaction to fungal spores on exposure, are often diagnosed as suffering from pneumonia.

In many instances, it is only after a lengthy attempt at treatment of an unresponsive respiratory problem that other causes and treatments are considered. The acute case of farmer's lung is not difficult to diagnose provided a proper history is taken. A subacute response to the spores can be diagnosed by antibody response from a blood sample. Other interactions with respiratory insults such as silo gas and other allergens should be considered. This is particularly of significance in the beef, dairy and pork producers.

An evaluation of the prevalence of farmer's lung, including acute and subacute cases, among individuals in the Ontario agriculture community has yet to be done and is a high priority for research. It is important to know that if the disorder is undiagnosed and chronic exposure continues an increasingly severe and irreversible lung fibrosis may occur. Again physician education is of prime importance and in keeping

with a recommendation of this report, farmer's lung is a high priority topic for this type of educational intervention. Improved diagnostic and treatment capabilities among Ontario physicians would lead to further recognition and prevention of this common problem.

Grain handlers diseases is a topic well researched both in Ontario and the Prairie Provinces in Canada. Broder (1984) has investigated the respiratory health of workers in grain elevators before and soon after they were hired. The findings indicate the occurence of a change in the respiratory status after a relatively brief duration of employment. The presence of phenol in grain dust extract leads to the formation of what appears to be a tannin-like material which accounts for the IgG precipitating activity and much complement fixing activity. This may be indicative of the type of reaction that is implicated in this lung disease.

Many large epidemiological studies by Cotton (1983), Warren and Manfreda (1983) and Dosman (1981 and 1977) have been done which has documented decrement in lung function tests as well as increased symptomology and lung disease among grain farmers. Similar studies by Chan-Yeung (1981) among grain elevator workers in Vancouver documented the prevalence of respiratory symptoms and lung function findings. Adjustment was made for smoking habits among grain workers the decline of lung function was not correlated with the initial lung function, presence of respiratory symptoms, atopic status, or duration of exposure. It was, however, correlated with acute changes in lung function over the course of one work shift and one work week. The conclusion was that grain dust has a deleterious affect on lung function of workers and should not be regarded as a nuisance dust.

Silo-filler disease is only part of a major hazard that is posed by silos on Ontario farms. In the modern air-tight silo (harvestore), fermentation of corn produces carbon dioxide consuming the available oxygen in the process. Within a short period of time there may be no detectable oxygen within the unit.

A person entering the silo may lose consciousness almost immediately, so quickly in fact that he is probably incapable of saving himself, even if he recognizes that he is in trouble. The hazard in the non-airtight tower silo is different. Degradation of the silo contents produces nitrogen dioxide gas and carbon dioxide. The nitrogen dioxide forms a layer on top of the ensilaged fodder. Above this layer, which may be of variable depth is normal air. Thus, an individual preparing to enter the silo from above encounters breathable air and may be misled into believing that the atmosphere within the silo is safe. Only after dropping down to the top of the fodder does he encounter the oxygen depleted air and nitrogen dioxide. Illness in which the symptoms do not manifest themselves for several hours may follow inhalation of sublethal concentrations of nitrogen dioxide. Worker education with regards to these types of hazards is paramount to the prevention of these disasters.

Farm workers on hog farms may be at risk of developing respiratory problems related to exposure to manure gases. Gas is heavier than air and collects in a tank or pit either in the confinement unit or outside. Agitation occurs during mechanical movement of the waste releasing noxious gases such as hydrogen sulphide. The study by O'Blenis (1984) done in Ontario explored a number of occupational health problems which include lung problems. A variety of exposures including airborne dust, ammonia, carbon dioxide, hydrogen sulphide, methane and carbon monoxide was considered. It was recommended that to draw further conclusions about decline in respiratory functions, a repeat survey must be carried out at a later date. Donham (1984) has initiated a survey of respiratory function in swine confinement buildings. Initially, a high prevalence of chronic respiratory disease has been documented and further research is required.

Reaction to mushroom spores can result in mushroom worker's lung. Even though a specific antigen has not been identified, a hypersensitivity reaction which can result in severe lung fibrosis and alveolitis may result. Removal of contact from the compost was necessary to limit the progression of the disease. Among tobacco workers, tobacco sickness characterized by a

feeling of generalized weakness followed by severe nausea and protracted vomiting is caused by absorption of nicotine from the green leaves of tobacco.

The scope of respiratory diseases among farm workers in Ontario is wide spread and requires greater awareness among physicians as well as farm workers. Specific conditions such as farmer's lung are often mistaken for other conditions and education programs directed at physicians in rural areas would hopefully alleviate some of the under recognition of this problem. Preventive interventions such as improved ventilation can be carried out and approved respiratory protective devices can be distributed where necessary. Over long periods of time however, these devices may not be comfortable and compliance would decrease especially on long hot summer days. Certain individuals have difficulty wearing them or breathing through them. Knowledge of the type of hazard and the risk to health may serve to increase compliance with these devices.

Further research is required to document the prevalence and extent of diseases such as farmer's lung in Ontario. Since most of these communities are served largely by family physicians, a sentinal physician system, whereby designated family physicians would report to a central source and monitor the trends of the newly recognized diseases, could improve the surveillance of these disorders. A similar system has been used for monitoring infectious diseases in Ontario.

Problem 6 - Infectious Diseases

Several types of animal-borne diseases are common among farm workers and will be described as follows.

Leptospirosis is a disease that mimics influenza consisting of fevers, chills, headaches, backaches, muscle tenderness, nausea, vomitting and lethargy. This occurs through direct or cindirect contact with infected cattle or hogs as well as contact with abortion tissues, feces, slurry, urine, contaminated waters

and soil.

Salmonella produces diarrhea, mild inflammation of the stomach and gastrointestinal tract and blood poisoning. The organisms are commonly found in sheep, calves, turkeys, chicken, swine, and dogs. Contact with infected animals as well as their feces and urine and contaminated egg powder or raw eggs can transmit this disease.

Brucellosis results in an acute syndrome consisting of weakness, chills, malaise, headache and joint pain and a chronic picture of malaise, headaches, sweating, vague pains and insomnia. Abscesses may develop in the liver, spleen, bone marrow, testes, ovary, kidney and brain. It is a common cause of abortion in cattle and premature delivery in goats and sows. The disease can be transmitted to humans either through ingestion or handling of infected milk, dairy products or meat, and handling aborted tissues.

Tuleremia consists of headache, chills, vomiting, aching, pains and fever. Enlarged glands and ulcerated infections can occur. This results in a debilitating disease in sheep. Rabbits and hares behave oddly, run slowly and appear to be tame. Tick bites or direct contact with infected animals as well as handling rabid carcasses and drinking infected water transmits this disease.

Q fever consists of severe headache, malaise, muscular pain and loss of appetite. Patchy infiltration of the lungs can occur. This occurs from direct or indirect contact with infected animals, wool, birth fluids, feces, urine, and drinking unpasteurized milk. Also, the agent can survive a drying process which leads to dust inhalation and infection.

Ornithosis consists of headache, chills, fever, anorexia, sore throat, nausea and vomitting which may progress to severe lung disease and respiratory failure. Contact with duck and turkey infected feces, feathers, aerosols during removal of bowel and entrails can result in this disease.

Toxoplasmosis results in fairly mild symptoms or perinatal infection and abortion, brain calcification, fever, jaundice and convulsions. Exposure to calf feces and eating infected under cooked meat may result in this disease. Anorexia, lethargy, high fever and death in cats, birds and other animals can be observed.

Fungal diseases such as blastomycosis result in lesions of the skin and lungs and severe infections of kidney, liver and spleen. This results from inhaling soil fungii of plowed soil. Similarly histoplasmosis in a severe form results in fever, anaemia, enlargement of spleen and liver, ulcers of the gastro-intestinal tract and a pulmonary disease resembling tuberculosis. Aerosols from abandoned chicken coops as well as inhaled soil fungii can cause the disease.

Pssitiacosis results in a cough, fever, severe headaches, chills, chest and back ache, and vomiting all may be asymptomatic. It may pose severe complications for pregnant women. Exposure to poultry and sheep directly or through dried saliva or fecal aerosol, birth fluids or a bite of a bird may result in this disease.

Most of these diseases are reportable in the Province of Ontario and as long as the reporting system is adequate, the Ministry of Health will continue to be capable of monitoring the trends of these types of diseases across various regions in Ontario. Close cooperation must be maintained between farm workers, farmers, veterinarians and public health personnel to maintain adequate surveillance of these types of diseases. The effective elimination or treatment of infected animals is paramount to prevention of further cases or outbreaks of these diseases. The current public health system is well suited to maintaining surveillance of infectious diseases among farm workers and further worker education will enhance the reporting of these diseases. Family physicians may regard some of these as exotic diseases, however, many may easily misdiagnose them as common colds and flus. Specific diagnostic tests through the

public health laboratories can more definitively establish the diagnosis and are readily accessible through the public health system. Education of family physicians again is paramount to enhancing the recognition of infectious diseases related to farm work.

Problem 7 - Noise-Induced Hearing Loss

The investigation of exposure to noise from agriculture equipment began by the group in Nebraska by Lierle (1959). The increasing mechanization of farm work including the increase of time of riding tractors has led to a general increase in the exposure time experienced by farmers to noise.

The effect of noise on the human body has been well investigated. There is a gradual decline in hearing sensitivity and this can be measured by serial audiometry. An increase in hearing thresholds across the high frequencies maximum at the three and four thousand cycles per second is observed. The symptoms of hearing loss include increasing difficulty in communication, tinnitus or ringing in the ears, difficulty with understanding speech especially in noisy environments, increasing irritability, headaches, and possibly psychological disorders. Increasing deafness may also be related to an increased risk of accidents as the detection of warning signals or malfunctioning machines may be impaired.

The site of damage to the hearing mechanism is at the cochlea, the delicate end organ mechanism deep in the temporal bone. Hair cells are disrupted and bent irreversibly, like wheat being blown on the prairies. The permanent effects of noise are often subtle and are not recognized initially by the worker themselves. Often the problem is identified by family members who become frustrated with their inability to communicate effectively with the person. The problem of tinnitus is problematic as very little medical therapy can alleviate the problem and results in a continuous irritation to the individual. Noise-induced hearing loss is an irreversible problem form which rehabilitation is only moderately successful in treating.

Hearing aids are often not effective in regaining communication abilities, and even after much expense to the individual, they are not used to their optimum capabilities.

The extent of the problem of hearing loss among farmers has been explored by a number of investigators including Thelin (1983), Sullivan (1981), McCarthy (1981). All of these studies point to the noise sources as being machines that are becoming larger and more powerful, as the size of farms increase and the demand for mass crop production rises. The measurement of sound, for example, from tractor noises is easily carried out by dosimeters that are readily available. The measurement of impact noise is somewhat more difficult and requires more sophisticated instrumentation.

The possibilities for preventing noise-induced hearing loss consist of primarily engineering controls by quieting the noise source from the diesel motors, enclosure of the farm worker by providing a cab on the tractor which can often be combined with air conditioning, and less preferably the use of personal protective devices such as ear plugs and ear muffs. The reason that these latter strategies are less effective is that compliance rates among workers are usually very low because of the discomfort of wearing them for many hours, up to 16 hours during peak harvest season. Exposure limits should be restricted to 85 db or less as this is at the level that is generally accepted that noise-induced hearing loss can be caused over a normal 40 hour working week and 40 year work career period. Current legislation in Ontario rests at 90 db for 8 hours per day and engineering controls may be instituted only where feasible.

There does not exist in the published literature a comprehensive survey of noise-induced hearing loss amongst agricultural workers in Ontario. This needs to be done to measure the extent of the problem and investigate efficient methods of controlling and preventing the effects of noise. Noise is soon to be a designated substance in the Province of Ontario and it will be important that agriculture workers are

included in this legislation. There are many sources of types of noise which should be assessed, not only that of mechanized equipment. For example, in the study of O'Blenis (1984) the noise exposure from pigs in confinement buildings was exceedingly high and posed a risk to pig farmers. In this situation engineering controls may not be feasible and stress on the compliance with the use of hearing protective devices must be made to those workers exposed. Even with optimum usage, the attenuation afforded by these devices often amounts to only 10 to 15 decibels over an extended period of wearing them and depending on the type and level of the noise exposure, this may not be sufficient to prevent some damage to the sensitive hearing apparatus. The effects of noise on the farming population may in fact, be a larger problem than one would expect. This clearly is a high research priority for Ontario to further understand the extent and distribution of noise problems in this working sector and that preventive measures can be taken once the problem is clearly recognized. The noise regulations, if applied to farm workers, could prevent many cases of this irreversible and isolating condition.

Problem 8 - Musculo Skeletal Diseases

Musculo skeletal diseases among farm workers include the major problem of low back pain as well as problems related to repetitive motion and adverse ergonomic conditions.

The problem of low back pain in industry is widespread and it is to be expected that this condition among farmers is a major problem. A number of ergonomic assessments have been carried out, notably by Sjoflot (1984) and Matthews (1983). The crucial factors related to mechanized equipment are the quality of the seating for the operator of the machine and the minimization of exposure to whole-body vibration. There is increasing evidence that exposure to this type of low-dose cumulative trauma can result in long-term effects on the discs of the spine resulting in degeneration and possibly herniation. Also strenuous work involving types of manual labour such as picking and lifting objects are common among farmers and often

result in repeated temporary disability from strains and muscle spasms.

Sepplainen (1977) reported a peroneal nerve palsy from strawberry picking. These types of problems can be expected in Ontario, especially in harvest season where there is a major incentive to work long hours at a very rapid pace. The only treatment for these types of diseases is that of rest, however, usually under the pressures of harvesting, the common musculo-skeletal problems are dismissed for economic reasons.

Prevention of vibration-induced disease, either to the whole body or to the extremeties such as the feet and hands, can be resolved by engineering controls and ergonomic solutions. Avoidance of awkward designs for tractors and other machinery should be considered carefully at the engineering stage. The natural history of musculo-skeletal disease is one of long-term disability that has been well recognized among farm workers in general, but not well measured in any large scale epidemiological study in Ontario.

Problem 9 - Accidents

Farming is well known to be a dangerous occupation. As mentioned previously, the character and the pace of farming in Ontario has changed dramatically in the past 20 years with the heavy mechanization and enlargement of the farming operations. A key study of farm accidents was done by Baker (1981) who reviewed the extent, scope and severity of accidents and injuries in Ontario. Although the hazards and dangers of farming have been long recognized, little research into the determinants and consequences of farm accidents have actually taken place. It has been implied that farmers are accident prone by various governments and accident prevention associations in the province, however, the evidence in the little research that has been done demonstrates that this is not the case. There appears to be a strong inverse relationship between the length of farming experience and the involvement in accident and injury. The

relationship to the tractor is central to the causation of many farm accidents. Other machines such as the grain auger have been singled out as a very dangerous machine.

The Workers' Compensation Board in Ontario reports that in 1983 there were 2,812 injuries to paid employees on 25,533 farms; roughly one injury for every 9 participating farms. The weighted average claim was $3,352, which represents a total outlay of 9.4 million dollars to these workers. There is no available data to estimate the amount of lost time experienced by the larger number of employer or self-accounting farmers or their families.

A number of issues are clear after reviewing this information. The tractor is the main agent of death and severe disability on Ontario farms. Mandatory installation of rollover protection devices on both new and old tractors would greatly reduce the number of fatalities. These devices are now mandatory in many European countries. Mandatory shielding of power take-off units and of machinery such as the auger would greatly reduce the number and severity of injuries that these instruments are capable of producing. Inexperience and immaturity are a factor in accident etiology. Educational programs such as those promoted by the farm safety association, although impossible to evaluate objectively, can only be encouraged in the strongest possible terms.

Accidents to children are occuring at an alarming rate. These children are often operating dangerous machinery or vehicles. Legislation governing the age of persons that may operate these types of machines should be brought into effect. The overall burden of non-fatal injuries on Ontario farms is impossible to assess given the information accrued. Every year there is possibly one accident for every 5 to 7 farms. If more accurate data is desired, then a comprehensive cohort study across the province would be required.

Problem 10 - Stress

The problem of stress and farm work has become a matter of increasing concern in recent years. Financial concerns and difficulties, lack of leisure time, lack of money for a holiday, and family responsibilities conflicting with farm expenditures were all related to increasing stress especially among woman farm workers. The women on the farm bear the burden of a number of different roles including family responsibilities as well as being responsible for financial decisions. The financial burdens therefore, would rest on the woman in the family and results in the bind of denying family members items that would normally be granted.

Mental fatigue and frustration were common symptoms as well as irritability. In more extremes sleeplessness and frank depression was encountered. Ireland (1981 and 1983) has described these factors involved in stress among farm workers very clearly in her research. In contrast Pfeiffer (1984) only surveyed aspects of lifestyle fitness among Ontario dairy farmers. From a number of variables the farmers enjoyed a number of health advantages over their urban peers. This clearly reflects the vigorous nature of farm work especially among males. The toll of stress however, is not seen in the type of measurements which can be done through anthropometric, physiological and psychosensory variables. The measurement of stress is difficult and must rely on the reports of psychological well being from the individuals concerned.

This is contrasted by a number of studies which look at the prevalence of psychiatric disease and symptoms amongst farm workers. This gives a different picture to the nature of stress-related disorders and also may be implicated in elevated rates of ischemic heart disease, even though more rigorous and nonanalytic studies have not been carried out. Other factors such as alcohol and drug abuse may be important as correlates of stress related problems.

The financial plight of the farm worker and farmer has been described in other documentation and will not be reviewed here. Clearly this is a major source of difficulty in this group and must be considered in any program to reduce the amount of stress-related problems.

Preventive Strategies

The development of mechanization and automation and of the use of chemical products and biological preparations during recent years have brought essential changes to agricultural work. It has made physical work somewhat lighter, but increased the risk of accidents, poisoning, and allergies. This situation is particularly acute in areas such as Ontario where workers may be exposed simultaneously to both traditional and new biological, physical and chemical factors.

Health and Safety conditions in agricultural work are determined by certain distinctive features of agricultural production such as:

1) the seasonal nature of the work and consequent urgency of certain tasks such as harvesting, which must be carried out rapidly and necessitates not only long working days, but also the employment of also a considerable seasonal work force;

2) the fact that work is carried out for the most part in open air, exposing the workers to different climatic and meteorological conditions depending on the season and climatic zone;

3) frequent changes in the type of task carried out by the same person, particularly in small scale enterprises where duties cannot be strictly defined and it is difficult to provide regular periods of work and rest;

4) multiple contacts with animals and plants which may give rise to infectious parasitic diseases, bites or other accidents due to animals, exposure to dust containing spores or other fungal allergenic matter or to toxic or irritant vegetable saps;

5) the use of a large variety of agricultural chemicals (pesticides, fertilizers, fungicides, herbicides, seed dressings) presenting a serious hazard of poisoning by skin absorption or inhalation;

6) the considerable distances between living quarters and work places, example where there are extensive pastures, which entail a great expenditure of energy and time, and the present risk of commuting accidents, disturbed eating habits, and render medical surveillance difficult;

7) the often primitive conditions of life, particularly on small farms where the work places and living quarters are under the same roof, and where sanitary conditions are sometimes unsatisfactory;

8) the large variety of working methods, the same task being performed either manually or mechanically depending on the level of economic development of the farm, local habits or size of the farm, with consequent differences in degree or risk;

9) the difficulty of imposing and complying with occupational safety and health standards and regulations on small farms;

10) the frequent employment of casual seasonal labour without any real occupational qualifications and ill-informed of risks and preventive measures, and also the frequent use of children to work on small farms.

These features pose major challenges to policy makers faced with designing programs and legislation and aimed at protecting the farmer, farmer's family and farm workers. The risk to health from farm work is considerable and the above barriers to effective preventive interventions must be overcome.

The use of some types of pesticides causes much emotive response in the general public. There is no doubt that harmful effects can influence the ecology of a region where pesticides are applied, and these undesirable features have to be weighed against the benefits that will result from their use. While the principles for the use of pesticides remain the same for all compounds, the stringency with which they must be applied depends

on the toxicity of the particular chemical.

The following points should be taken into account:

(a) The toxicity of the chemical.

Acute toxicity is measured by the $LD_{50}$ value; this is a statistical estimate of the number of mg of the chemical per kg of body weight required to kill 50% of a large population of test animals. The dose may be administered by a number of routes, usually orally or dermally, and the rat is the standard test animal. Oral or dermal $LD_{50}$ values are used according to which route has the lower value for a specific chemical. Other effects, either as a result of short-term exposure such as neurotoxicity or mutagenicity, or of long-term exposure such as carcinogenicity, have to be taken into account, but pesticides with such known properties should not be registered for use. The WHO Recommended Classification of Pesticides by Hazard classifies technical products according to the acute risk to human health as follows: Class 1A: extremely hazardous, Class 1B: highly hazardous, Class 11: moderaterly hazardous, Class 111: slightly hazardous, Class IV: technical products unlikely to present any acute hazard in normal use. Technical products at present are identified only by chemical trade name, and not classified under the WHO Recommended Classification of Pesticides by Hazard.

(b) The method of use.

Poisons enter the body through the mouth , the lungs, the intact skin or wounds in the skin. The inhalation hazard is determined by the physical form and solubility of the chemical. The possibility and degree of skin absorption varies with the chemical, but some chemicals also exert a direct action on the skin, causing dermatitis. Pesticides are applied in many different forms: as solids, by spraying in dilute or concentrated form, as dusts (fine or granulated), and as fogs and gases. The method of use has a bearing on the

likelihood of absorption.

(c) The route of absorption.

The dermal $LD_{50}$ value is obtained when the animal is poisoned by the chemical being painted on shaven skin. For practical purposes, dermal or percutaneous absorption of a chemical is more important than oral absorption in occupational situations.

(d) The vehicle in which the chemical is applied.

The chemical may be mixed with solids (often with food used as bait), water, kerosene, oils, or organic solvents. Some of these diluents have some degree of toxicity of their own and may influence the rate of absorption of the pesticide chemical.

(e) The formulation.

Many formulations contain other chemicals which are not themselves pesticides but which enhance the effectiveness of the pesticide. Added surface-active agents are a case in point. When two or more pesticides are mixed in the same formulation, the action of one or both may be enhanced by the presence of the other. In many cases, the combined effects of mixtures have not been fully worked out, and it is a good rule that mixtures should always be treated as more toxic than any of the constituents on their own.

Preventive interventions and policies must address the following issues with regard to chemical hazards:

(a) Availability.

The toxicity of many pesticides is such that their indiscriminate use by the general public is certain to result in many people being affected, often fatally. It is

therefore essential that the public should have restricted access to all formulations except those that are only slightly hazardous. In many countries this requirement is covered under the poisons legislation. The purchase of compounds of moderate or high hazard should be restricted to commercial users, and the use of extremely hazardous compounds should be limited to operators who are trained and licensed. It is important to specify in legislation that the restrictions apply not only to the sale of these compounds but also to gift and barter.

(b) Transportation.

In a number of well documented cases, large numbers of people have been affected after consuming constituents of foodstuffs (commonly flour, sugar or rice), which have been contaminated by pesticides during transportation. Pesticides of any degree of toxicity should be transported in containers which are clearly labelled, leak-proof and not easily damaged. They should never be transported beside or above any type of food, and all spillages should be immediately reported. Any foodstuff transported in the same compartment as a pesticide may thus be held, pending examination to ensure that it has not been in any way contaminated.

(c) Labelling.

The requirements regarding the labelling of pesticides should be laid down in legislation and strictly applied to both imported and locally produced chemicals. The label should give the following essential information: both the approved name and the trade name of the chemical; the name of the manufacturer, packager or supplier; the directions for use; the precautions to be taken during use, including details of protective equipment to be worn; the symptoms of poisoning; the firstaid treatment for suspected poisoning.

The greater the degree of toxicity or hazard of the

chemical, the more precise should be the wording on the label. It is sound practice for the different classes to be clearly distinguished by background colours on the label and, in the case of compounds of high or extreme hazard, for the appropriate danger symbol to be incorporated.

It often occurs that an adequately labelled quantity of pesticide in bulk is locally repacked into smaller containers. Each such small package should bear a similar label, and repacking in containers which have held, or are easily identifiable with, containers used for food should be absolutely forbidden. If small packages are to be transported, the same rules apply as for the carriage of larger packages.

(d) Storage.

The principles set out under "Transportation" above also apply to storage. Pesticides of moderate or higher hazard should be so stored that only authorised persons can have access to them. It is particularly important that children should be excluded from any contact with pesticide concentrates or residues. Spillages often occur in storage and repacking rooms, and must be cleaned up with care.

Rooms used for storage only should be soundly constructed and fitted with secure locks. Floors should be kept clear and the pesticides clearly identified. If repacking is carried out in storage rooms, adequate light should be available; floors should be impervious and sound; washing facilities should be available; and eating, drinking and smoking should be prohibited in the area.

A few compounds react with other chemicals or with air, and this has to be taken into account when planning storage facilities. Examples are cyanide salts (which react with acid to produce hydrogen cyanide gas) and dichlorvos (which vaporises in contact with air).

(e) Uses

(i) Training

While all workers using pesticide formulations of moderate or higher hazard should be thoroughly trained in their use, such training is particularly important if the pesticide is extremely toxic. Training programmes should cover: toxicity of compounds used and routes of absorption; handling of concentrates and formulations; methods of use; cleansing of equipment; precautions to be taken and protective equipment to be worn; maintenance of protective equipment; avoidance of contamination of other crops, foods, and water supplies; early symptoms of poisoning; first-aid measures to be taken.

All training should be strictly relevant to the pesticide actually being used and, in the case of extremely hazardous compounds, it is wise to license operators following an examination to show that they have in fact, a good understanding of the hazards and the procedures to be followed.

(ii) Mixing

This is possibly the most hazardous phase of the use of pesticides, since the worker is exposed to the concentrate. In any particular situation, selected men only should be responsible for mixing; they should be thoroughly conversant with the hazards and provided with the proper facilities for dealing with accidental contamination. Even when the mixed formulation is of such a toxicity that it can be used with a minimum of protective equipment, more elaborate equipment may need to be provided for and used by the mixer.

(iii) Application

For pesticides of moderate or higher hazard, some type of protective equipment is almost always necessary. The choice of particular items of equipment will depend on the hazard of the pesticide and the physical form in which it is being handled. Any consideration of protective equipment must also include not only provision but also adequate cleansing, maintenance and replacement. Where climatic

conditions preclude the use of some types of protective equipment, three other principles of protection can be applied, i.e. protection by distance; protection by time; protection by change of working method.

Protection by distance involves modification of the equipment used for application, so that the man is far away as possible from from the pesticide itself, bearing in mind the likely routes of absorption of a specific compound. Protection by time involves limitation of hours of work. The suitability of this method depends on whether the pesticide is readily excreted or whether it is cumulative. Cumulation of some compounds occurs in the body when the rate of excretion is slower than the rate of absorption. With some other compounds, a cumulation of effect may occur when the man is exposed to repeated small doses which, taken individually, may not give rise to symptoms.

Protection by change of working method involves a reconsideration of the whole operation. Pesticides differ from other industrial processes in that they can be applied from the ground or the air. Changes of method on the ground depend largely on the choice of equipment and the physical nature of the pesticide to be applied.

Pesticides are applied from the air as liquids, dusts or granules. Liquids may be sprayed from very low altitudes, frequently as fine droplets of concentrated formulations, known as ultra-low volume (ULV) applications. Drift is a problem particularly with liquids and dusts. Aerial application is an economical way of treating large tracts of land but entails special hazards to pilots and to workers on the ground.

Pilots can be affected by leakage from hoppers, by pesticide carried into the cockpit on clothes and boots, and by flying back through the swathe just released or through the drift from the swathe. Even minor degrees of absorption of some pesticides or their local effects (such as may be caused, for instance, by an organophosphorus compound in the eye) can affect a pilot to the extent that he cannot maintain the high

degree of vigilance necessary for low flying. Pilots should not be allowed to engage in pesticide operations unless they have been specially trained in the items listed under (i) above, in addition to any special aviation and agricultural operational requirements.

On the ground, loaders and flagmen may be affected. The same principles apply to loaders as to others dealing with pesticides in bulk. Flagmen mark the swathe to be flown and can be severely contaminated if the pilot misjudges the moment of release. Ballons or flags can be placed in position before or ahead of the operation and workers should never be used as flagmen within the flight pattern.

(iv) Public health measures

When pesticides are used, every effort must be made to avoid contamination of water supplies, whether these are officially recognised supplies or not. This not only concerns the actual application (when there may be immediate contamination) but must also include consideration of remote contamination by run-off through rainfall on recently treated areas.

While pesticides in natural watercourses may be diluted to such a degree that the contaminated water may not be hazardous in itself, the effect on fish, on water vegetables used as food and grown in watercourses, and on wild life as a whole must not be overlooked. Such hazards may be economic rather than directly related to health but are no less important.

(v) Other restrictions

The hazards associated with pesticides do not end with their application; with the more toxic compounds it has been shown that there is a danger to workers entering a sprayed crop too soon after application. It is therefore important that all workers and members of the general public should be informed concerning the areas where a toxic pesticide has been applied, and the earliest date on which it is safe to enter and work in these areas. Where a food crop has been sprayed, it is also important that the crop should not be harvested until a sufficient

period has elapsed for degradation of the pesticide to take place, in order to avoid excessive residues on food.

(f) Disposal of pesticides and containers.

Spillages of pesticides at any stage of their storage or handling should be treated with great care. Liquid formulations may be reduced to solid phase by evaporation. Dry sweeping of solids is always hazardous: these should be removed by vacuum cleaning or by dissolving them in water or other solvent in the factory environment. In the field they may be washed away with water into a suitable soak-hole. Contaminated top-soil should be removed and buried if any domestic animals or fowls are in the are. Soak-holes should be used for disposing of washing waters from cleaning application equipment, clothing or hands. These should be at least 30 cm deep and sited well away from wells or watercourses.

Empty pesticide containers should be collected with care, or disposed of safely. Plastic liners, and paper or card containers should be crushed and buried well below top soil or burned, preferably in an incinerator. Metal containers of some pesticides can be decontaminated according to the instructions of the pesticide manufacturers. Such drums should be clearly marked "Not to be used for food or for water for drinking or domestic use". Other metal containers should be punctured, crushed or buried.

(g) Hygiene

Where a pesticide is of moderate or higher hazard and can be readily absorbed through the skin, special precautions are necessary. In some situations where men may become accidentally contaminated with large quantities of concentrate, such as in factory situations and mixing, it is necessary to provide a shower bath in addition to the usual washing facilities. Special arrangements for cleansing clothing and overalls may be

necessary; in any case, these should not be left for the worker to wash at home.

Since pesticides are often applied outside the factory environment, depending on the chemical used, special care may have to be taken to provide washing facilities at the workplace, even though this may be in remote fields. Workers should be encouraged to use these rather than bathe themselves in canals and rivers, the water from which may be subsequently used for other purposes; the washing water provided should be disposed of with care as outlined above. Smoking, eating and drinking before washing should be absolutely prohibited when any pesticide of moderate or higher toxicity is being handled or used.

(h) Medical and first aid facilities.

Where an antidote exists which can be readily used as a first-aid measure for a specific pesticide (e.g. atropine for organophosphorus poisoning). It should be readily available to workers who should be instructed in the method of its use. When any pesticide is being used on a substantial scale, doctors in the area should be informed by the persons responsible for distribution. The nature of the chemical used should be well defined so that the doctors can obtain specific antidotes where these are applicable and be on the watch for cases of poisoning. Facilities should also be available to these doctors for differential diagnosis, even if these are of the simplest type, such as tests for determining cholinesterase levels. Strict routine medical supervision of workers heavily exposed to concentrates, as in the manufacture and packing of pesticides, is essential and should include laboratory tests.

In the medical selection of workers to deal with pesticides of moderate or higher hazard, apart from consideration of the physical requirements involved, some assessment of intelligence, personal hygiene and sense of responsibility is also indicated. The decline in use of DDT and some other

organochlorine pesticides has resulted in the use of other pesticides of higher acute toxicity and therefore, in most cases, of higher hazard. Emphasis has to be laid on education at all levels so that the maximum human and economic benefit can result from the use of these chemicals.

Policy Options for Prevention

The first decision for Ontario policy makers concerns whether prevention is seen and organised as an integral part of treatment and care services, or whether it needs its own organisational structure. This is an old problem for which there are no easy answers. Briefly, the arguments in favour of an integrated administration with treatment and care services are that many doctors, nurses and other health workers have a contribution to make to prevention and that prevention needs the backing of this treatment sector. The arguments in favour of a separate organisation of preventive services relate to the special needs of the agricultural sector. The current treatment and care services in Ontario often relegate prevention to a secondary role.

At the present time, if the hazards to health in the social and economic environments are to be more effectively tackled new forms of organisation seem to be necessary. To bring a preventive perspective to agricultural economic policy, multidisciplinary contributions are needed. Social science skills are just as important as those in the medical or physical sciences. The local level is, however, also important because here prevention workers are needed to monitor and deal with peculiarly local problems. This level is also more subject to the local demands and preferences which should guide health action.

In conclusion, five clear recommendations have arisen from this literature review and analysis.

RECOMMENDATION 1

A detailed survey regarding exposure to pesticides and organic chemicals in farm work be carried out across Ontario to identify populations at risk of adverse health effects.

RECOMMENDATION 2

A health data collection system for agricultural health and safety be established to detect potential adverse health effects of farm work in Ontario.

RECOMMENDATION 3

An agricultural health and safety research program be organized within an Ontario University to carry out descriptive and analytical epidemiological studies of the health of persons engaged in farm work.

RECOMMENDATION 4

An intensive educational program for family physicians, medical officers of health, physicians in postgraduate training, and medical and nursing students concerning occupational health and safety in agriculture be initiated in Ontario.

RECOMMENDATION 5

Preventive interventions including legislation and community-based worker education pertaining to the protection of the health of persons engaged in farm work in Ontario be brought into effect.

These represent first steps to improve our understanding of the health of persons engaged in farm work in Ontario and to protect and promote the most valuable resource in this economic sector, the health of farmers, farmer's families and farm workers.

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